In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: June 24, 2019

LINDA PARKER,	*	No. 14-979V
Petitioner,	*	Special Master Sanders
v.	*	Entitlement Hearing; Influenza ("Flu") Vaccine; Rheumatoid Arthritis ("RA"); Polyarticular Inflammation; *Althen* Causation
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

William Cochran, Jr., Black McLaren Jones Ryland & Griffee, PC, Memphis, TN, for Petitioner.
Lisa A. Watts, United States Department of Justice, Washington, D.C., for Respondent.

DECISION ON ENTITLEMENT[1]

On October 14, 2014, Linda Parker ("Petitioner") filed a petition pursuant to the National Vaccine Injury Compensation Program.[2] Petitioner alleged that the influenza ("flu") vaccine that she received on October 19, 2013, caused her to develop rheumatoid arthritis ("RA") and polyarticular inflammation. Pet. at 1, ECF No. 1

After carefully analyzing and weighing all of the evidence and testimony presented in this case in accordance with the applicable legal standards, I find that Petitioner has not met her legal burden. Petitioner has failed to provide preponderant evidence that the flu vaccine she received on October 19, 2013, caused her to develop RA or polyarticular inflammation. Accordingly, Petitioner is not entitled to compensation.

[1] This decision shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet**. In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. (hereinafter "Vaccine Act," "the Act," or "the Program").

I. Procedural History

Petitioner filed her petition on October 14, 2014, ECF No. 1, and the case was then assigned to Special Master Dorsey. *See* ECF No. 4. Over the following four months, Petitioner filed fifteen exhibits consisting of medical records and affidavits, *see* Pet'r's Exs. 1–15, ECF Nos. 7-1–7-6, 8-2–8-6, 10-2–10-6, as well as a statement of completion on March 27, 2015. ECF No. 12. Respondent filed his Rule 4(c) report and two pieces of medical literature on July 10, 2015. *See* Resp't's Report, ECF No. 22; Resp't's Exs. A–B, ECF Nos. 22-1–22-2. Special Master Dorsey ordered Petitioner to file an expert report by November 30, 2015. ECF No. 26.

This case was reassigned to Special Master Roth on October 21, 2015. *See* ECF No. 27. Over the next eight months, Petitioner filed three motions for extensions of time, extending her deadline to file an expert report until July 1, 2016. *See* ECF Nos. 29–31; *see also* Non-PDF Orders, docketed Nov. 24, 2015, Feb. 25, 2016, Apr. 28, 2016. On June 10, 2016, Petitioner filed an expert report authored by Dr. Paul J. Utz and six pieces of supporting medical literature. Pet'r's Exs. 17–24, ECF Nos. 32-1–32-8.

Respondent filed an expert report authored by Dr. Mehdad Matloubian on November 14, 2016. Resp't's Exs. C–D, ECF Nos. 34-1–34-2. On January 23, 2017, Respondent filed thirty-seven pieces of medical literature via compact disk. *See* Resp't's Exs. E–OO, ECF No. 36. Petitioner filed a supplemental expert report from Dr. Utz and five pieces of supporting medical literature on March 22, 2017, Pet'r's Exs. 25–30, ECF Nos. 37-1–37-6, and additional medical records on June 6, 2016. Pet'r's Exs. 31–36, ECF Nos. 39-1–39-6.

This case was reassigned to me on June 20, 2017. *See* ECF No. 40. On August 10, 2017, I issued an order scheduling an entitlement hearing for April 16–17, 2018. ECF No. 43. On January 19, 2018, Petitioner filed her opening prehearing brief. ECF No. 46. Respondent filed his responsive prehearing brief and one piece of medical literature on February 20, 2018. ECF No. 48; Resp't's Ex. PP, ECF No. 48-1. Petitioner filed her reply prehearing brief on March 23, 2018. ECF No. 54. Petitioner also filed a second supplemental expert report authored by Dr. Utz and five pieces of supporting medical literature on this date. Pet'r's Exs. 44–49, ECF Nos. 55-1–55-6.

On April 2, 2018, Respondent contacted Chambers to request a status conference. Informal Comm., docketed Apr. 2, 2018. I held a status conference with the parties on April 4, 2018, where Respondent indicated that Petitioner's expert report filed on March 23, 2018, raised "several new arguments" and that "his expert w[ould] not be able to respond to the new arguments prior to the hearing, and w[ould] likely not be prepared to respond to the arguments at the hearing if it proceed[ed] as scheduled." ECF No. 57. I agreed with Respondent and "expressed concern that the hearing may not be productive if Respondent's expert ha[d] not had an opportunity to review the newly-raised arguments." *Id.* Therefore, I rescheduled the entitlement hearing for August 16–17, 2018, and ordered Respondent to file a response to Petitioner's second supplemental expert report by May 10, 2018. ECF No. 59. On May 9, 2018, Respondent filed a responsive supplemental expert report authored by Dr. Matloubian and five pieces of supporting medical literature. Resp't's Exs. UU; UU Tabs 1–5, ECF Nos. 62-1–66-5.

On August 13, 2018, Petitioner filed a motion to admit late-filed medical literature at the hearing, ECF No. 64, and two additional pieces of medical literature. Pet'r's Exs. 51–52, ECF Nos. 63-1–63-2. Respondent filed his response on August 14, 2018, in which he argued that "Petitioner's motion fail[ed] to articulate reasonable, much less 'compelling' circumstances for the relief sought . . . and should properly be denied." ECF No. 65. I granted Petitioner's motion on August 14, 2018, because "there [was] good cause to grant [the] motion and admit the exhibits" and "their admission w[ould] not unfairly prejudice Respondent." ECF No. 66 at 1–2. I permitted Respondent to "introduce, if necessary, literature which directly address[ed] the specific issues addressed by Petitioner's Exhibits 51 and 52 at any time before his expert testifie[ed]." *Id.* at 1. Respondent filed one piece of medical literature in response to this Order on August 15, 2018. *See* Resp't's Ex. VV, ECF No. 67-1.

I held an entitlement hearing on August 16–17, 2018. *See* Min. Entry, docketed Aug. 20, 2018. The parties have not filed any post hearing briefing. *See* docket. This matter is now ripe for consideration.

II. Factual Background

A. Pre Vaccination

Although Petitioner saw several different providers for various conditions unrelated to this claim, her pre vaccination records reflect no apparent chronic pain complaints. Her medical records document a few acute pain complaints related to injuries, such as an injury to her hand. *See* Pet'r's Ex. 8 at 21, ECF No. 8-3. She also complained of knee pain prior to her vaccination. A handwritten note from a March 28, 2012 visit with internist, Dr. Win Thu, reflects that Petitioner complained of "knee pain" in addition to other issues, some of which are illegible. Pet'r's Ex. 15 at 5, ECF No. 10-6. Dr. Thu's assessment and plan are likewise illegible in the note. *Id.*

Petitioner was also treated by Dr. Kent Wenger during the years prior to her vaccination. *See* Pet'r's Ex. 11, ECF No. 10-2. A note dated March 14, 2012, reflects that Dr. Wenger had been seeing Petitioner since 2006 for psychological treatment. *Id.* at 1. There are visit notes from twelve dates between 2010 and 2013 contained in the record. *Id.* at 3–6, 10–13. Although these notes are handwritten and difficult to read, most do not appear to contain any complaints of physical pain that would be potentially relevant to this case. However, there are two references to Petitioner's knees. The March 13, 2012 note reflects that Petitioner "hurt [her] knee." *Id.* at 12. The April 5, 2012 note reflects that Petitioner was doing "some walking" but that her "knees [were] in bad shape." *Id.* at 11. The note also contains the following: "need to exercise [illegible] hurts knees." *Id.* On the same date, Dr. Wenger noted that Petitioner "[d]eveloped an immune sensitivity to" a medication that she had previously taken. *Id.*

Petitioner's medical records reflect that she smoked every day.[3] *See, e.g.*, Pet'r's Ex. 4 at 2, ECF No. 7-4. Petitioner was a lab technician at Putnam Community Medical Center. Pet'r's Ex. 6 at 2, ECF No. 7-6.

B. Vaccination

Petitioner received a seasonal flu vaccination in her left deltoid on October 19, 2013. Pet'r's Ex. 2. ECF No. 7-2.

C. Post Vaccination

1. Petitioner's Affidavits

Petitioner stated in her first affidavit that she experienced soreness in her left shoulder one day post vaccination, on October 20, 2013. Pet'r's Ex. 1 at ¶ 4, ECF No. 7-1. Petitioner stated that the pain spread to both shoulders, and eventually to her knees, hips, groin, wrists, and hands. *Id.*

In Petitioner's second affidavit, she further stated that by October 21, 2013, her left shoulder was weak, and the pain was "severe and interfered with [her] ability to sleep." Pet'r's Ex. 12 at ¶ 4, ECF No. 10-3. Petitioner then explained that "[b]etween October 21, 2013, and November 1, 2013, the pain and weakness in [her] left shoulder subsided to some extent but did not go away." *Id.* at ¶ 5. Petitioner noted that during that time period, "the type of pain [she] was experiencing in [her] left shoulder began to appear in [her] right shoulder." *Id.* Petitioner grew "quite distressed" and on November 1, 2013, she left work to go to the emergency room for evaluation. *Id.* at ¶ 6. At that time, she "was experiencing pain in both shoulders that seemed to be radiating from [her] shoulders to [her] chest." *Id.* Petitioner then stated that those symptoms "continued, and [she] also began experiencing intermittent pain in [her] knees and wrists as well as back pain, swelling in [her] extremities, and muscle aches." *Id.* at ¶ 7.

Petitioner described additional symptoms that she began to experience "[a]fter November 1, 2013." *Id.* at ¶¶ 9–10. She stated that she experienced groin pain, which she reported to a provider on April 3, 2014. *Id.* at ¶ 9. She further stated that she began to experience pain in her hips and swelling in her right hand, which she reported to a provider on April 16, 2014. *Id.* at ¶ 10. Petitioner also asserted in her affidavit that she used a cane to assist with walking during the visit on April 16, 2014. *Id.*

2. Medical Records

The first medical record after Petitioner's vaccination is from November 1, 2013. On that date, Petitioner presented to the Putnam Community Medical Center Emergency Department. Pet'r's Ex. 3, ECF No. 7-3; *see also* Pet'r's Ex. 10a at 36–50, ECF No. 8-5. The "Principal

[3] On an intake form dated April 16, 2014, Petitioner confirmed that she smoked one pack of cigarettes per day. Pet'r's Ex. 6 at 8. In a December 6, 2017 note, a provider documented that Petitioner had been smoking one pack of cigarettes per day since 1975. Pet'r's Ex. 41 at 7, ECF No. 49-5.

Admitting Diagnosis/Reason for Visit" listed on the registration form for that visit is "high blood pressure." Pet'r's Ex. 3 at 1. The nurses' notes reflect that Petitioner complained of "pain in [her] left lateral posterior chest and right lateral posterior chest," as well as nausea upon presentation. *Id.* at 19. Notes also reflect that Petitioner complained of "pain in [her] back[,]" which "radiate[d] to [her] chest" and was "aching." *Id.* at 20. Petitioner reported that the pain began one week prior and was intermittent; at its worst, the pain was a ten out of ten on a pain scale. *Id.* Petitioner reported substernal area chest pain at five out of ten on a pain scale. *Id.* Petitioner also reported shortness of breath at rest, nausea, and anorexia. *Id.* The emergency department physician documented that Petitioner discovered that she had high blood pressure at a physician's office and was also complaining of bilateral shoulder pain. *Id.* at 16. The physician's examination revealed "mild pain in both shoulder joints on external rotation" and anxiety. *Id.* at 17. Ultimately, Petitioner was discharged the same day in stable condition, with a diagnosis of hypokalemia[4] and weakness. *Id.* at 18, 22. She was advised to follow up in one week. *Id.* at 18.

On December 18, 2013, Petitioner saw Dr. Wenger for psychiatric therapy. Pet'r's Ex. 11 at 3. Dr. Wenger documented in the note from that date that Petitioner reported increased pain since receiving the flu vaccine in October. *Id.* He also noted that the pain had "spread out from there (l[eft] arm)" and by this visit was in the right arm and both knees. *Id.* He wrote that it was "excruciating (!)" pain. *Id.* Parts of Dr. Wenger's notes are difficult to read, but he appears to have noted Petitioner's flu shot and pain, accompanied by several "?" notations, suggesting that he was unsure of a cause or correlation. *Id.* Under the plan section of the note, Dr. Wenger circled "support" and wrote "not hypochondriac – see rheum." *Id.* A medication list from this visit indicates that Petitioner was taking Toradol,[5] although it is unclear whether Dr. Wenger prescribed the medication to Petitioner or whether she reported that she was taking the medication from some other source at that time. *Id.* at 7.

On January 12, 2014, Petitioner presented to the Putnam Community Medical Center Emergency Department with complaints of lower back pain after a fall at work. Pet'r's Ex. 10 at 24. Petitioner reported that she fell from an upright position six and a half hours before she presented to the emergency department. *Id.* at 26. She complained of lower back pain with movement, and the physician documented that her pain was mild, while range of motion ("ROM") was painful and muscle spasm was noted in the left and right lower back. *Id.* Imaging showed degenerative disc changes but no acute abnormalities. *Id.* at 25. The nurses' notes reflect that Petitioner also complained of a left knee injury, although only the lower back complaints were documented by the physician. *Id.* at 29. Petitioner was discharged home with a diagnosis of a lumbar spine sprain. *Id.* at 27. She was prescribed Toradol and instructed to follow up with a private physician for further care. *Id.* at 27, 31–32.

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[4] Hypokalemia is the "presence of an abnormally low concentration of potassium ions in the circulating blood." *Hypokalemia*, STEDMANS MEDICAL DICTIONARY 429130 (2014).

[5] Toradol (ketorolac tromethamine) is "a nonsteroidal anti-inflammatory drug (NSAID), [which] is indicated for the 'short-term' (up to 5 days in adults), management of moderately severe acute pain that requires analgesia at the opioid level and only as continuation treatment following IV or IM dosing of ketorolac tromethamine, if necessary." Roche Pharmaceuticals, *Toradol Oral Medicine Label* (2013), *https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/019645s019lbl.pdf.*

Three days later, on January 15, 2014, Petitioner presented to the Putnam Community Medical Center Emergency Department with wrist pain that began two or three days prior. *Id.* at 15, 21. Petitioner reported decreased ROM and pain in her right wrist due to a fall at work four days prior. *Id.* at 17. The physician's note reflects that Petitioner was previously evaluated for the fall at work, but she did not mention an issue with her wrist at that time. *Id.* The physician observed "injury or acute deformity, swelling, [and] tenderness" in Petitioner's right wrist. *Id.* Imaging reflected no fracture, dislocation, or instability of the wrist. *Id.* at 16. Petitioner was discharged with a diagnosis of a contusion. *Id.* at 19, 22. She was prescribed Tylenol-Codeine #3[6] and was advised to follow up with orthopedics in two or three days. *Id.* at 22–23.

Two days later, on January 17, 2014, Petitioner saw Physician's Assistant ("PA") David C. Cox at Medical Express ("MedEx") complaining of joint pain. Pet'r's Ex. 4 at 1–5. The PA documented that Petitioner reported intermittent joint pain in both shoulders and knees, as well as her right wrist. *Id.* at 2. Petitioner also reported that the pain "started after flu inj[ection]" and was becoming more frequent. *Id.* The note reflects Petitioner reported walking as an aggravating factor for her pain, while Toradol and Tylenol #3 were alleviating factors. *Id.* The PA also documented that Petitioner complained of "muscle aches, arthralgias/joint pain, back pain, and swelling in the extremities." *Id.* Upon examination, he found that Petitioner was anxious and depressed, and documented normal motor strength but with "tenderness and limited ROM" in "Joints, Bone, and Muscles." *Id.* at 2–3. He did not specify to which joints, bones, and/or muscles those findings applied. *Id.* Petitioner declined lab studies during the visit. *Id.* at 3. The PA diagnosed unspecified joint pain and prescribed ketorolac[7] intramuscularly, Mobic[8] tablets, and prednisone tablets.[9] *Id.* Petitioner was instructed to follow up with another doctor. *Id.*

On January 22, 2014, Petitioner followed up with Dr. Alex M. Pulido at Pulido Internal Medicine. Pet'r's Ex. 5, ECF No. 7-5. The visit note from that date reflects that the reason for the appointment was to establish a new primary care provider. *Id.* at 3. In the review of symptoms, Dr. Pulido documented that Petitioner denied carpal tunnel syndrome, joint stiffness, leg cramps, muscle aches, pain in shoulder(s), painful joints, sciatics, swollen joints, trauma to arm(s), trauma to hip(s), trauma to knee(s), trauma to ankles(s), and weakness. *Id.* at 5. Although there were no abnormal findings documented in the examination portion of the note, Dr. Pulido assessed hypertension, hyperlipidemia, diverticulitis of colon, obesity, personal history of tobacco use, and "unspecified polyarthropathy or polyarthritis, multiple sites." *Id.* at

[6] Tylenol-Codeine #3 is a "combination of medication . . . used to help relieve mild to moderate pain. It contains an opioid . . . pain reliever (codeine) and a non-opioid pain reliever (acetaminophen)." TYLENOL-CODEINE NO.3, https://www.webmd.com/drugs/2/drug-3179/tylenol-codeine-3-oral/details (last visited June 7, 2019).

[7] Ketorolac tromethamine is "a nonsteroidal anti-inflammatory drug administered intramuscularly, intravenously, or orally for short-term management of pain[.]" *Dorland's* at 984.

[8] Mobic is a brand name for meloxicam, an NSAID used in the treatment of osteoarthritis. *Dorland's* at 1126, 1171.

[9] Prednisone is "a synthetic glucocorticoid derived from cortisone, administered orally as an anti-inflammatory and immunosuppressant in a wide variety of disorders." *Dorland's* at 1509.

3. Dr. Pulido ordered testing, including rheumatoid factor ("RF"),[10] erythrocyte sedimentation rate ("ESR"),[11] antinuclear antibodies ("ANA")[12] w/Reflex if Positive,[13] and creatine phosphokinase ("CPK").[14] *Id.* at 4. Petitioner's labs were negative for ANA and RF, but she had a high ESR of 47 and a CPK level of 30. *Id.* at 8–10; Pet'r's Ex. 10 at 12–14. A cardio CRP-high sensitivity test reflected a level of 25.3 mg/L. Pet'r's Ex. 5 at 10; Pet'r's Ex. 10 at 11.

Petitioner cancelled an appointment scheduled with Dr. Pulido for February 5, 2014. Pet'r's Ex. 5 at 7.

On March 25, 2014, Petitioner submitted a report to the Department of Health and Human Services ("HHS") Vaccine Adverse Event Reporting System ("VAERS") regarding the flu vaccine she received on October 19, 2013. Pet'r's Ex. 9, ECF No. 8-4. A letter from HHS to Petitioner reflects that some items were missing from the VAERS report, and HHS asked Petitioner to submit additional information. *Id.* However, only one page of the letter is contained in the record, and it is unclear what information was identified as missing. *Id.* It is also unclear whether Petitioner responded to the letter.

On April 3, 2014, Petitioner returned to MedEx and saw Dr. Shirine S. Gharda. Pet'r's Ex. 4 at 6–9. Petitioner's chief complaint at this visit was a "[r]ight knee problem." *Id.* at 6. She reported one day of constant right knee pain at a level of five out of ten, which was alleviated with ice. *Id.* at 7. The doctor noted that Petitioner also had swelling and right shoulder and right groin pain. *Id.* Dr. Gharda further documented the following: "migratory polyarthralgias with swelling since [O]ct[ober] 2013[;] initial[] work up showed elevated [ESR] and [CRP;] having flare needs prednisone. To go see rheumatologist." *Id.* In another section of the note, Dr. Gharda wrote that Petitioner reported "arthralgias/joint pain (right knee and left shoulder pain and swelling for 2 days)." *Id.* Upon exam, Dr. Gharda noted "erythema,[15] swelling, and warmth (to right knee)." *Id.* at 8. However, Dr. Gharda also noted "normal motor strength . . . normal movement of all extremities and no tenderness," and no edema. *Id.* Petitioner was prescribed prednisone tablets, Solu-Medrol[16] for injection, and ketorolac tablets. *Id.* She was instructed to follow up with a rheumatologist and return as needed. *Id.*

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[10] Rheumatoid factor tests for "antibodies directed against antigenic determinants . . . in the Fc region of the IgG class of immunoglobulins." *Dorland's* at 676. These antibodies "are found in the serum of about 80 percent of persons with classical or definite [RA]." *Id.*

[11] Erythrocyte sedimentation rate measures "the rate at which erythrocytes precipitate out from a well-mixed specimen of venous blood, measured by the distance the top of the column of erythrocytes falls in a given time interval under specified conditions[.]" *Dorland's* at 1594.

[12] Antinuclear antibodies are "antibodies directed against nuclear antigens; ones against a variety of different antigens are . . . frequently found in [RA.]" *Dorland's* at 101.

[13] A reflex test "occurs when an initial test meets pre-determined criteria . . . and the primary test result is inconclusive[.]" *Reflex Testing*, TRIHEALTH LABORATORIES, https://apps.trihealth.com/trihealthlab/Reflex%20Testing.pdf (last visited June 10, 2019).

[14] Creatine phosphokinase (AKA creatine kinase) is "an Mg^{2+}-activated enzyme of the transferase class that catalyzes the phosphorylation of creatine by ATP to form phosphocreatine." *Dorland's* at 429.

[15] Erythema is "redness of the skin produced by congestion of the capillaries." *Dorland's* at 643.

[16] Solu-Medrol is the "trademark for preparation of methylprednisolone sodium succinate." *Dorland's* at 1731.

On April 16, 2014, Petitioner saw Dr. T. Mark Lloyd at the Southeastern Integrated Medical ("SIMED") Southeastern Arthritis Center. Pet'r's Ex. 6 at 1–15. On a medical history form, Petitioner reported her symptoms as "[p]ain [and] inflam[m]ation in all joints." *Id.* at 2. During the visit, the doctor documented in Petitioner's history of present illness that she had a "migratory polyarthritis" since October 2013, which "ha[d] involved shoulders/hips/knees and most recently swelling in her [right] hand." *Id.* at 11. He wrote that Petitioner "to date has a +CRP only/neg[ative] serologies," and had responded to high dose steroids. *Id.* Dr. Lloyd noted that Petitioner's "only [history] [wa]s a flu shot the day before this started." *Id.* He wrote that Petitioner's hips were sore and stiff on that date, but that her hands were "qauiet," presumably a typo intended to reflect that Petitioner's hands were "quiet." *Id.*; *see id.* at 16 (containing a nearly identical history of present illness note). Dr. Lloyd listed "symmetric polyarticular inflammation" as an "active problem" for Petitioner. *Id.* Notes from the physical examination do not reflect any significant abnormalities. *Id.* at 12–13. Dr. Lloyd ordered lab work and prescribed Medrol. *Id.* at 13–14.

Petitioner presented to Putnam Community Medical Center for the lab work. Pet'r's Ex. 6 at 21–28; Pet'r's Ex. 10 at 3–6. Petitioner's lab work reflects that she was again negative for the RF and ANA. Pet'r's Ex. 6 at 22; Pet'r's Ex. 10 at 5–6. Her cyclic citrullinated peptides[17] ("CCP") result was 97, and the lab results indicate that any result above 59 represents a "strong positive." Pet'r's Ex. 6 at 22; Pet'r's Ex. 10 at 6. Petitioner's ESR was 64. Pet'r's Ex. 6 at 25; Pet'r's Ex. 10 at 4. Her C-reactive protein ("CRP")[18] result was 11. Pet'r's Ex. 6 at 28; Pet'r's Ex. 10 at 3.

A letter in Petitioner's file dated April 18, 2014 and authored by Dr. Lloyd reflects that Petitioner was "having trouble walking and [would] need to be excused from work for at least [three] days due to her medical condition." Pet'r's Ex. 6 at 29.

Petitioner returned to see Dr. Lloyd on May 7, 2014. Pet'r's Ex. 6 at 16–20. Dr. Lloyd's history of present illness note is essentially the same as the prior visit. *Id.* at 16. In this note, Dr. Lloyd listed "drug monitoring of medications" and "[RA]" along with "symmetric polyarticular inflammation" in Petitioner's "active problems" list. *Id.* In a "therapy" portion of the visit note, Dr. Lloyd documented the results of Petitioner's CCP, ESR, and CRP results and noted that he would reduce the Medrol dose and start methotrexate.[19] *Id.* at 19. Dr. Lloyd also documented that he discussed concerns about tobacco use with Petitioner. *Id.*

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[17] Citrullination is "a posttranslational modification of proteins in which peptideylarginine deiminase catalyzes the conversion of arginine residues to citrulline residues. . . . [I]t also occurs in a variety of inflammatory conditions." *Dorland's* at 366. A posttranslational modification is an alteration "to protein structure that take[s] place after synthesis." *Id.* at 1503. In genetics, such modification refers to "the process by which the series of codons (triplet bases) in a messenger RNA (mRNA) is converted to the ordered sequence of amino acids that constitutes a specific polypeptide chain." *Id.* at 1953.

[18] C-reactive protein is "a globulin that forms a precipitate with the somatic C-polysaccharide of the pneumococcus in vitro; it is the most predominant of the acute phase proteins." *Dorland's* at 1532.

[19] Methotrexate is "a folic acid antagonist that acts by inhibiting synthesis of DNA, RNA, thymidylate, and protein; used as an . . . antiarthritic in the treatment of . . . severe rheumatoid and psoriatic arthritis." *Dorland's* at 1151.

On July 2, 2014, Petitioner saw Dr. Wenger. Pet'r's Ex. 11 at 2. Although much of the note is difficult to read, it appears that Petitioner reported the history of her pain complaints and treatment with Dr. Lloyd. *Id.* She reported that she "missed a lot of work" due to pain. *Id.* Petitioner also reported problems with stress at work and told Dr. Wenger that she "hit a bear" and that her car was in the shop. *Id.*

On October 22, 2014, Petitioner saw Dr. Gharda. Pet'r's Ex. 13 at 1–11, ECF No. 10-4. The note from that visit reflects that Petitioner reported that she had no primary care provider. *Id.* Petitioner's chief complaint was "pain." *Id.* Dr. Gharda noted that Petitioner was diagnosed with RA in August of 2014[20] and "ha[d] seen [a] rheumatologist for migrating joint pain and swelling with redness." *Id.* Dr. Gharda further noted that Petitioner "[t]ried methotrexate and could not tolerate it[, and was then] on prednisone[, w]ith frequent flares." *Id.* Dr. Gharda reported that Petitioner was requesting a "referral to Shands [Hospital/University of Florida] rheumatology." *Id.* at 1. Petitioner reported "muscle aches, arthralgias/joint pain, and swelling in the extremities." *Id.* at 2–3. An examination revealed "tenderness (to heel, yesterday to knee)." *Id.* at 3. Dr. Gharda provided a referral to rheumatology, with the following "Note to Provider: long history of po[l]yarthrthra[]lgias, with joint swelling and redness with diagnosis of RA[;] resistant to methotrexate, on prednisone. Concerned something else might be going on." *Id.* at 3. Dr. Gharda also provided a prescription for Percocet.[21] *Id.* at 3, 7.

On December 11, 2014, Petitioner had a visit with Dr. Adrian Vazquez at University of Florida Health. *Id.* at 13–16; *see also* Pet'r's Ex. 14 at 11–14, ECF No. 10-5. At this visit, Dr. Vazquez included a lengthy summary of the history of present illness. Pet'r's Ex. 13 at 14. In that summary, Dr. Vazquez wrote that Petitioner described her lab results and "report[ed] . . . that in fall 2013 she began having left shoulder pain then it migrated to the right shoulder then knees, feet and hands became involved. [She also reported] [h]and involvement including MCPs[22]/PIPs[23] with associated swelling, warmth, erythema, and [morning] stiffness [for about one] hour. [Petitioner described her] [p]ain as constant, aching, 7/10 pain unless she was on prednisone or Medrol." *Id.* Dr. Vazquez also wrote that Petitioner showed him a picture of her right hand, which revealed "swelling/erythema of MCPs particularly 2nd-3rd MCPs." *Id.* Dr. Vazquez described the medications that Petitioner had tried, including prednisone and methotrexate. *Id.* He noted that Petitioner was taking Medrol 16 mg per day, which "controlled her joint pain/swelling," but that she was "self-medicating as she never returned to see Dr. Lloyd." *Id.* The visit note reflects that Petitioner was smoking one and a half packs of cigarettes per day at this time. *Id.* at 15. Dr. Vazquez "[s]uspect[ed] [that Petitioner] has [RA] based on history,[24] picture of [her right] hand and reported +CCP Ab." Pet'r's Ex. 14 at 13. Differential

[20] The last visit note from Dr. Lloyd was dated May 7, 2014. Pet'r's Ex. 6 at 16–20. There are no records reflecting a diagnosis or visit with any medical providers in August of 2014.

[21] Percocet is the "trademark for a combination preparation of oxycodone hydrochloride and acetaminophen." *Dorland's* at 1409.

[22] Metacarpophalangeal joints (MCPs) are those "pertaining to the metacarpus and phalanges," or the hand and fingers. *Dorland's* at 1142.

[23] Proximal interphalangeal joints (PIPs) are the joints between the first and second phalanges, or bones in one's fingers. *See Dorland's* at 950, 973.

[24] There is no mention of the August 2014 diagnosis referenced by Dr. Gharda.

diagnoses included seronegative spondylarthritis ("SpA"),[25] crystal arthritides,[26] and osteoarthritis.[27] *Id.* He also noted that Petitioner was at risk for osteopenia[28]/osteoporosis[29] because she had been taking "moderate-high doses of corticosteroids" for more than a year. *Id.* Dr. Vazquez documented that Petitioner's exam was normal but opined that her symptoms were "likely masked by Medrol 16mg" per day. *Id.* Dr. Vazquez counseled Petitioner "on the importance of smoking cessation" and noted that smoking is "likely worsening her arthritis." *Id.* He ordered labs and imaging. Pet'r's Ex. 13 at 16; Pet'r's Ex. 14 at 14.

Imaging was completed on the same day. An x-ray of the cervical spine showed "[n]o specific evidence for inflammatory arthritis." Pet'r's Ex. 14 at 2. X-rays of the right and left hands and feet revealed "[n]o specific radiographic evidence for inflammatory arthritis" but did show "mild osteoarthritis of the bilateral hands and feet." *Id.* at 2–8. Additionally, the x-rays showed a "[s]mall radiopaque foreign body in the left foot on the plantar surface of the distal first phalanx." *Id.*

On January 8, 2014, Petitioner presented to the Putnam Community Medical Center for additional diagnostic testing. Pet'r's Ex. 31 at 52, ECF No. 39-1. The order reflects that Petitioner was to be evaluated for "inflammatory arthritis, atlantoaxial[30] instability, crowned dens syndrome,[31] and osteoarthritis." *Id.* at 56. A bone densitometry scan ("DEXA")[32] was performed. *Id.* at 58–59. The report indicates that the test was compared with a prior test from October 27, 2010. *Id.* at 58. The report reflects the following impressions: "(1) The patient has osteopenic bone mineral density; (2) When compared to the young adult population, the patient's fracture category is: moderate; (3) Compared to the prior study the patient's bone mineral density has decreased significantly in the hips and mildly in the lumbar spine." *Id.*

On January 13, 2015, Petitioner followed up with Dr. Vazquez. Pet'r's Ex. 14 at 8–11. Dr. Vazquez noted that Petitioner's bilateral hand pain had "improved." *Id.* at 8. Petitioner's main complaint on this date was "bilateral knee pain worse with ambulation but improved with rest and diffuse muscle pain that lasts all day." *Id.* Dr. Vazquez noted that he did not yet have

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[25] Spondylarthritis is "arthritis of the spine." *Dorland's* at 1753.
[26] Crystal arthritides (AKA crystal-induced arthritis) is "arthritis due to the deposition of inorganic crystalline material within the joints[.]" *Dorland's* at 150.
[27] Osteoarthritis is "a noninflammatory degenerative joint disease seen mainly in older persons, characterized by degeneration of the articular cartilage, hypertrophy of bone at the margins, and changes in the synovial membrane." *Dorland's* at 1344.
[28] Osteopenia is "1. [A]ny decrease in bone mass below normal. 2. [R]educed bone mass due to decrease in the rate of osteogenesis to the extent that there is insufficient compensation for normal bone lysis." *Dorland's* at 1347–48.
[29] Osteoporosis is "reduction in bone mineral density, leading to fractures after minimal trauma." *Dorland's* at 1348.
[30] Atlantoaxial means "pertaining to the atlas and the axis." *Dorland's* at 173. The atlas is "the first cervical vertebra, which articulates above the occipital bone and below with the axis." *Id.* The axis is "the second cervical vertebra[.]" *Id.* at 185.
[31] Crowned dens syndrome is "crystal-induced arthritis around the dens axis, often accompanied by fever and neck pain." *Dorland's* at 1826.
[32] A bone densitometry scan determines one's "bone mineral density," and is "used in the diagnosis and management of conditions such as osteogenesis imperfecta and osteoporosis." *Dorland's* at 487.

the results of the DEXA scan. *Id.* In the physical examination portion of the note, Dr. Vazquez documented that there was synovial[33] thickening over the right second MCP joint, bilateral patellar crepitus,[34] and diffuse myofascial tenderness to light touch. *Id.* at 9. Dr. Vazquez diagnosed Petitioner with uncontrolled seropositive RA and stable osteoarthritis. *Id.* at 10–11. He also diagnosed diffuse myofascial pain syndrome,[35] which he noted was "likely secondary to chronic depression/anxiety and sleep issues." *Id.* at 10. He noted that "[f]ibromyalgia is often caused [and] exacerbated by untreated depression and/or sleep disorders" and suggested that Petitioner might benefit from a change in certain medications prescribed by her psychiatrist or primary care physician. *Id.* at 11. Dr. Vazquez also discussed the risks and potential benefits of Enbrel,[36] and Petitioner agreed to initiate therapy with that medication to treat her seropositive RA. *Id.* at 10–11.

Petitioner had a visit with Dr. Wenger on January 21, 2015. Pet'r's Ex. 33 at 6, ECF No. 39-3. Dr. Wenger noted that Petitioner was "still on steroids," which helped her walk and use her hands but also caused hair loss and weight gain. *Id.* Dr. Wenger documented that Petitioner saw Dr. Vazquez, who suggested a medication change to Enbrel and a different psychiatric medication. *Id.* Dr. Wenger wrote that he had some concern with the proposed substitute in Petitioner's psychiatric medication due to Petitioner's history but still planned to add it to Petitioner's regimen. *Id.*

Petitioner saw Dr. Wenger again on February 25, 2015. *Id.* at 5. Dr. Wenger documented in his note that Petitioner had not yet started Enbrel due to "insurance barriers." *Id.* He noted that Petitioner had "pain chronic (RA)," which was not helped by the change of medicine suggested by Dr. Vazquez. *Id.* Petitioner also had a visit note dated March 12, 2015 in Dr. Wenger's records, but the note only reflects "n/s." *Id.* at 4. Petitioner saw Dr. Wenger again on April 1, 2015, and April 22, 2015. *Id.* at 3–4. It does not appear from the notes that Dr. Wenger documented anything related to pain or movement difficulties on either date. *Id.*

Petitioner presented to the Putnam Community Medical Center for lab work on July 3, 2015. Pet'r's Ex. 16, ECF No. 23-1; *see also* Pet'r's Ex. 31 at 31–51. On that date, Petitioner's RA factor result was flagged as high. Pet'r's Ex. 16 at 1. The report lists the reference interval for the test as 0.0–13.9 IU/ml, and Petitioner's result was 184.4 IU/ml. *Id.* at 1, 10. CCP

[33] Synovial is defined as "pertaining to the synovium . . . or secreting synovia." *Dorland's* at 1855. The synovium is "membrana synovalis capsulae articularis." *Id.* at 1856. Synovia is "a transparent alkaline viscid fluid, resembling the white of an egg, secreted by the synovial membrane, and contained in joint cavities, bursae, and tendon sheaths." *Id.* at 1855.

[34] Joint crepitus is "the grating sensation caused by the rubbing together of the dry synovial surfaces of the joints." *Dorland's* at 429. The patella is "a triangular sesamoid bone . . . situated at the front of the knee in the tendon of insertion of the quadriceps extensor femoris muscle." *Id.* at 1395.

[35] Myofascial pain syndrome "is a chronic pain condition affecting the musculoskeletal system." *What is Myofascial Pain Syndrome?*, HEALTHLINE, https://www.healthline.com/health/myofascial-pain (last visited June 10, 2019).

[36] Enbrel is a brand name for etanercept, "a soluble tumor necrosis factor receptor that inactivates tumor necrosis factor," which "is used in the treatment of [RA]." *Dorland's* at 612, 650.

Antibodies immunoglobulin G ("IgG")/immunoglobulin A ("IgA")[37] were high, at 80 units. *Id.* at 1. Anything higher than 59 in that test is considered to be a "strong positive." *Id.* Petitioner's complement[38] C3 and C4[39] serum were within the reference intervals, but her total complement (CH50) was high at 65 U/mL, where the reference interval is 42–62. *Id.* Petitioner tested negative for ANA. *Id.* at 1, 10. A serum protein electrophoresis was "essentially unremarkable." *Id.* at 2. Myeloma ("M-spike") protein[40] was flagged as high at 0.1 g/dL, and the reference interval indicates "not observed." *Id.* at 3. Petitioner had high hemoglobulin ("HGB"),[41] hematocrit ("HCT"),[42] and mean corpuscular hemoglobulin ("MCH")[43] in her complete blood count ("CBC")[44] panel. *Id.* at 6. Her ESR was also high, at 33 mm/hr. *Id.* at 7.

Petitioner presented to the Putnam County Medical Center Emergency Department late in the evening on October 30, 2015. Pet'r's Ex. 31 at 1–30. On the admission form, the "principal admitting diagnosis/reason for visit" is listed as "back pain." *Id.* at 1. An "attestation statement" from the same admission reveals that the diagnosis at admission was "cough," the principal diagnosis was "bronchitis, not specified as acute or chronic," and secondary diagnoses were "essential (primary) hypertension" and "nicotine dependence, unspecified, uncomplicated." *Id.* at 9. The nurse who initially assessed Petitioner reported that she had "pain below the left shoulder blade [and a] nonproductive cough [for three] days with wheezing." *Id.* at 11. Petitioner reported her pain at a level seven intensity, and the nurse documented "back pain" as her chief complaint. *Id.* A chest x-ray was ordered due to the cough. *Id.* at 10. It revealed "no radiographic evidence of acute cardiopulmonary disease," but among the "findings" the report notes the following: "Bony thorax: Mild osteopenia with degenerative changes of the spine and shoulders." *Id.* Petitioner was discharged early the next day. *Id.* at 16. Clinical impressions at the time of discharge were primary, "bronchitis with bronchospasm" and secondary, "back pain."

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[37] IgG is "the principal class of antibody in the blood and extracellular fluid" that "opsonizes pathogens for engulfment by phagocytes and activates the compliment system[.]" KENNETH MURPHY & CASEY WEAVER, JANEWAY'S IMMUNOBIOLOGY 424 (9th ed. 2017). IgA "is the principal class [of antibody] in secretions" and "functions chiefly as a neutralizing agent." *Id.*

[38] Complement refers to "the entire functionally related system comprising at least [twenty] distinct serum proteins, their cellular receptors, and related regulatory that is the effector not only of immune cytolysis but also of other biologic functions[.]" *Dorland's* at 393.

[39] C3 is "a component of both the classical and alternative complement pathways[.]" *Dorland's* at 393. C4 is a "component of the classical complement pathway[.]" *Id.* at 394.

[40] Myeloma protein refers to "any of the pathological immunoglobulin proteins or fragments . . . secreted by myeloma cells." *Dorland's* at 1533.

[41] Hemoglobulin is "the red oxygen-carrying pigment of erythrocytes, formed by developing erythrocytes in bone marrow." *Dorland's* at 839.

[42] Hematocrit level measures "the proportion of the volume of a blood sample that is red blood cells . . . measured in mL per dL of whole blood or a percent." *Dorland's* at 832.

[43] Mean corpuscular hemoglobulin measures "the average hemoglobulin content of an erythrocyte[.]" *Dorland's* at 840.

[44] Complete blood count is "a series of tests of the peripheral blood that provide[s] a tremendous amount of information about the hematologic system and many other organ systems." KATHLEEN DESKA PAGANA & TIMOTHY J. PAGANA, MOSBY'S MANUAL OF DIAGNOSTIC AND LABORATORY TESTS 174 (5th ed. 2014).

Id. at 21. Petitioner was prescribed an albuterol[45] inhaler, ketorolac thromethamine[46] tablets, and prednisone tablets. *Id.* at 20.

Petitioner saw Dr. Wenger on November 10, 2015. Pet'r's Ex. 33 at 2. He documented in the visit note that Petitioner was "still on steroids" for "flares of R.A." *Id.*

On March 16, 2016, Petitioner presented to Dr. Myriame Vastey at Azalea Health to establish care for "[a]rthralgias and hypertension." Pet'r's Ex. 32, ECF No. 39-2. Petitioner reported the onset of arthralgias as two years prior, specifically identifying the location of the arthralgias in the bilateral hips. *Id.* at 1. Dr. Vastey noted that Petitioner was diagnosed with RA two years prior and was told that she may also have fibromyalgia. *Id.* She also noted that Petitioner had been treated with methylprednisolone[47] but was "out of med[ication]." *Id.* Dr. Vastey documented that Petitioner's hypertension was stable, and she only needed a medication refill. *Id.* Petitioner reported at this visit that she continued to smoke a pack of cigarettes per day and had done so for the last forty-one years. *Id.* Upon physical examination, Dr. Vastey noted bilateral knee crepitus, but no significant joint abnormalities. *Id.* at 3.

There are also blood test results in the record from March 16, 2016. Pet'r's Ex. 37 at 17–19, ECF No. 49-1. Petitioner's ANA screen was negative, whereas her RF result was 161 IU/mL, which was flagged as high. *Id.* at 17–18. Her ESR was 22 m/hr, which is within the range provided in the test of less than or equal to 30 mm/hr. *Id.* at 18.

On April 11, 2016, Petitioner presented to the Putnam Community Medical Center Emergency Department with pain in her right arm. Pet'r's Ex. 36 at 1, ECF No. 39-6. DO[48] Mark Sbarro documented that her chief complaint was an "exacerbation of ra" beginning that day. *Id.* at 2. In the physical exam portion of the note, the provider documented that tenderness was present in both the right and left hands. *Id.* at 4. He prescribed prednisone, ketorolac thromethamine, and acetaminophen/hydrocodone. *Id.* Petitioner was discharged after less than an hour. *Id.* at 9, 12.

Petitioner saw Dr. Vastey again on May 18, 2016. Pet'r's Ex. 34, ECF No. 39-4. At that visit, Dr. Vastey noted that Petitioner's hyperlipidemia started in 2010, and is associated with "joint pain and myalgia." *Id.* at 1. Dr. Vastey reported that Petitioner exhibited bilateral wrist arthralgias that were constant and fluctuated. *Id.* Dr. Vastey noted that Petitioner "had two RA flare up[s] since [her] last visit [two months prior] [and was] scheduled to see [a] rheumatologist [on] June 14." *Id.* Petitioner was instructed to follow up with her rheumatologist but was

[45] Albuterol is "a β-adrenergic agonist, specific for β_2-adrenergic receptors; administered by inhalation as a bronchodilator for the treatment and prophylaxis of bronchospasm associated with bronchitis . . . or other chronic obstructive airway disease[.]" *Dorland's* at 45.

[46] Thromethamine is another name for Toradol. *See Toradol*, RXLIST, https://www.rxlist.com/toradol-drug.htm (last visited June 10, 2019).

[47] Methylprednisolone is "a synthetic glucocorticoid derived from progesterone, used in replacement therapy for adrenocortical insufficiency and as an anti-inflammatory and immunosuppressant in a wide variety of disorders; administered orally." *Dorland's* at 1154.

[48] DO is an abbreviation for "Doctor of Osteopathy." *See* NEIL M. DAVIS, MEDICAL ABBREVIATIONS: 26,000 118 (12th ed. 2005).

prescribed methylprednisolone "in case of flare." *Id.* at 4. There are no records indicating that Petitioner followed up with a rheumatologist in June or any other time between this May 18, 2016 appointment and her next appointment with Dr. Vastey in July of 2017. *See* Pet'r's Ex. 34; Pet'r's Ex. 37.

Petitioner saw Dr. Wenger on May 24, 2016. Pet'r's Ex. 33 at 1. Much of the note is difficult to read, but he did note the "legal issue of flu shot related to R.A." in her record on that date. *Id.* It appears to be a note regarding releasing records to Petitioner's attorney, rather than an opinion regarding the merits of Petitioner's suit. *Id.* The record contains the results of a blood test from May 9, 2017. Petitioner's ANA screen was negative, and her RF was flagged as high at 161 IU/mL. *Id.* at 17–18.

On July 11, 2017, Petitioner saw Dr. Vastey. *Id.* at 1. Petitioner reported "acute symptoms of RA" and noted that symptoms had "progressed and she want[ed] to establish with rheumatology." *Id.* Dr. Vastey noted that steroids "work well with flares" but that Petitioner had "not taken [disease modifying antirheumatic drugs] DMARDS[49] due to concerns of side effects." *Id.* Petitioner reported that she continued to smoke a pack of cigarettes per day. *Id.* Dr. Vastey noted the use of a cane at this visit. *Id.* at 4. A note reflects that the plan was to refill the Medrol prescription, and that a referral to rheumatology was made on July 6, 2017. *Id.* at 4. Dr. Vastey noted that Petitioner "still ha[d fifteen] tabs of [P]ercocet." *Id.*

Petitioner presented to the Putnam Community Medical Center Emergency Department on August 28, 2017, for arthritis pain. Pet'r's Ex. 38 at 102–32, ECF No. 49-2. Dr. Gerry Meta documented that Petitioner complained of severe right and left wrist pain, which he described as an "RA FLARE." *Id.* at 112. The onset of pain was the same day and was rated as nine out of ten on a pain scale. *Id.* at 112, 117. Ketorolac tromethamine was administered intramuscularly. *Id.* at 122. Petitioner was also prescribed Percocet. *Id.* at 129.

On August 31, 2017, Petitioner saw PA Joseph Altamirando at Azela Health to follow up after the emergency room visit, which he noted was due to "another RA flare [involving] severe swelling of [her] right wrist." Pet'r's Ex. 37 at 1. PA Altamirando noted that Petitioner made an appointment with rheumatology for December and was unable to get an earlier appointment. *Id.* at 1, 9. PA Altamirando also documented that Petitioner reported that Toradol and prednisone "do help but she knows she cannot take [them] constantly." *Id.* PA Altamirando advised Petitioner to take steroids and Toradol "in brief regimens [of three to four] days, then remain off for as long as possible." *Id.* at 9.

On October 25, 2017, Petitioner presented to St. John's Family Care for left hip pain that started two weeks prior. Pet'r's Ex. 42 at 9, ECF No. 49-6. Petitioner reported that the pain was achy, moderate, and aggravated by movement. *Id.* Another portion of the note reflects that Petitioner "fe[lt] like [the hip] [wa]s broken." *Id.* at 11. An x-ray revealed no fractures or degenerative changes but did reveal "mild joint space narrowing." *Id.* at 10. Petitioner was prescribed Percocet for the pain. *Id.*

[49] Disease-modifying antirheumatic drugs "act on the immune system to slow the progression of [RA]." *Treating Rheumatoid Arthritis with Disease-Modifying Drugs (DMARDs)*, WEBMD, https://www.webmd.com/rheumatoid-arthritis/guide/dmard-rheumatoid-arthritis-treatment#1 (last visited June 10, 2019).

Petitioner reported back to Dr. Vastey on November 2, 2017 with complaints of back pain that started one week prior. Pet'r's Ex. 37 at 11. Petitioner also complained of left hip pain which had persisted for three weeks. *Id.* Petitioner reported that she had an x-ray the previous week but was told that the results were normal so "she would like an order for an MRI." *Id.* Petitioner reported that her pain was at a level of three out of ten. *Id.* at 13. Dr. Vastey ordered an x-ray of the lumbar spine and a urine drug screen.[50] *Id.* at 14. She also prescribed Percocet tablets to be taken twice daily "as needed for severe pain" and instructed Petitioner to follow up in two weeks. *Id.* The x-ray report impression was "[m]ild compression fracture at the superior endplate of L3. The age [was] uncertain. Bilateral facet joint arthropathy at L4-5 and L5-S1 with suspected neural foraminal stenosis."[51] *Id.* at 20; Pet'r's Ex. 38 at 6.

On November 14, 2017, Petitioner saw a nurse practitioner at Florida Neurosurgical Associates. Pet'r's Ex. 43 at 16–18, ECF No. 50-1. She complained of lumbar and left lower extremity pain that began approximately four weeks prior. *Id.* at 16. Petitioner told the provider that "she was sitting on the floor at work . . . and when she got up she felt a twing in her back." *Id.* Petitioner reported that she thought the pain was related to her RA, so she took a dose of steroids, but the pain did not improve. *Id.* The provider ordered an MRI. *Id.* at 17. A note authored by Dr. Eric W. Scott at Florida Neurosurgical Associates on November 15, 2017, reflects that x-rays and an MRI revealed an old fracture at L3, facet arthropathy, and a disc bulge, but no disc herniation or stenosis. *Id.* at 11, 14–15, 18. Dr. Scott documented that Petitioner's symptoms were "highly suggestive of primary hip joint disease and/or sacroiliitis,[52]" and he ordered an MRI of the left hip. *Id.*

An MRI of the left hip obtained on November 21, 2017, revealed "[m]oderately severe changes of femoral neck stress fracture;" "[m]oderately severe degenerative joint changes and associated synovitis;[53]" and "[m]ild insertional tendinosis[54] of the gluteus minimus/medius[55] and hamstring tendons." *Id.* at 8. Dr. Scott referred Petitioner to Dr. Timothy Lane for her left hip pain. Pet'r's Ex. 40 at 4–7, ECF No. 49-4; *see also* Pet'r's Ex. 43 at 2–4.

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[50] Petitioner's urine drug screen was positive for benzodiazepines. Pet'r Ex. 37 at 16. Alprazolam, which Petitioner had been prescribed by Dr. Wenger, is a benzodiazepine.

[51] Neural foraminal stenosis "is a type of spinal stenosis . . . [which] occurs when the small openings between the bones in [the] spine, called the neural foramina, narrow or tighten." *Neural Foraminal Stenosis*, HEALTHLINE, https://www.healthline.com/health/neural-foraminal-stenosis (last visited June 10, 2019).

[52] Sacroiliitis is "inflammation (arthritis) in the sacroiliac joint." *Dorland's* at 1662.

[53] Synovitis is "inflammation of a synovium; it is usually painful, particularly on motion, and is characterized by a fluctuating swelling due to effusion within a synovial sac." *Dorland's* at 1856.

[54] Insertional tendinopathy "is a common disorder caused by repetitive tendon strain and subsequent poor tendon healing." *Insertional Tendinopathy*, AMBOSS, https://www.amboss.com/us/knowledge/Insertional_tendinopathy (last visited June 10, 2019).

[55] The gluteus minimus muscle is located in the "lateral surface of [the] ilium between [the] anterior and inferior gluteus lines." The gluteus medius muscle is located in the "lateral surface of [the] ilium between [the] anterior and posterior gluteus lines." Both muscles "abduct[] and rotate[the] thigh medially." *Dorland's* at 1205.

Dr. Lane noted on November 28, 2017, that Petitioner "ha[d] had pain involving her left hip for six months to a year," which was "moderate in severity." Pet'r's Ex. 40 at 4. Dr. Lane further documented that around November 2, 2017, Petitioner had increased pain which caused difficulty at work and at home. *Id.* Dr. Lane ordered x-rays, which "reveal[ed] bone-on-bone changes present in the left hip and osteopenia." *Id.* at 6. He also reviewed the November 21, 2017 MRI, along with a Dr. Vogler, and determined that "the findings [were] consistent with avascular necrosis[56] of the femoral head[57] with an insufficiency fracture and bone edema extending into the intertrochanteric area[58] and femoral neck." *Id.* Dr. Lane documented that he discussed surgery with Petitioner, and she elected to proceed with total hip replacement. *Id.*

Petitioner was seen for a preoperative exam on December 1, 2017. *Id.* at 2. A CT scan and lab tests were completed. *Id.* at 8–9, 18. Petitioner had a total left hip replacement on December 6, 2017. *Id.* at 10–17; *see* Pet'r's Ex. 41 at 47. The surgical records reflect several diagnoses underlying the need for the surgery. Pet'r's Ex. 41 at 4 ("[r]heumatoid and osteoarthritis" and a "stress fracture" in the hip), 6 ("degenerative arthritis/avascular necrosis").

Kindred at Home ("KAH") provided in-home surgery aftercare starting on December 9, 2017. *See* Pet'r's Ex. 39, ECF No. 49-3. Petitioner followed up with Dr. Lane at The Orthopedic Institute on January 2, 2018. Pet'r's Ex. 40 at 1, 19. Although he noted that Petitioner was "walking well with and without her walker," he recommended continued use of the walker for another month. *Id.* The note reflects that Petitioner planned to return to work in March. *Id.*

On February 19, 2018, Petitioner had a rheumatology consultation with Dr. Annabelle Lee at Baptist Primary Care – South Rheumatology. Pet'r's Ex. 50 at 1–13, ECF No. 61-1. The note from that date reflects that Petitioner was referred by Dr. Lane "for consultation regarding elevated [RF]." *Id.* at 1. The history of present illness portion of the note reflects the following:

> [Petitioner] reportedly had symptoms as early as October 2013 [which] started [twenty-four] hours after she received a flu shot. She reportedly had [an] "extreme immune response" with pain on left shoulder associated with limited [ROM]. She took over-the-counter NSAIDs with symptoms resolving within a week. After that, she had migratory polyarthralgia involving right shoulder, left knee, right knee, both hands, ankles, and both hips. She ha[d] noted MCP swelling, redness, and warmth. She was empirically treated with prednisone which significantly helped. She had been tested for [RF] which was reportedly negative in the past.

Id. That section then reviews Petitioner's treatment history. *Id.* The note contains "Results/Data," but the formatting makes the data difficult to interpret. *Id.* at 3–11. Dr. Lee

[56] Avascular necrosis "is the death of bone tissue due to a lack of blood supply." *Avascular Necrosis*, MAYO CLINIC, https://www.mayoclinic.org/diseases-conditions/avascular-necrosis/symptoms-causes/syc-20369859 (last visited June 10, 2019).
[57] Femoral head (AKA caput femoris) is the "head of [the] femur." *Dorland's* at 286.
[58] The intertrochanteric area is "situated in or pertaining to the space between the greater and the lesser trochanter." *Dorland's* at 951.

assessed osteoarthritis and RA of the foot and hand. *Id.* at 11. Dr. Lee planned to check labs, obtain x-rays, continue with prednisone prescriptions, and follow up as indicated or necessary. *Id.* at 13.

Petitioner had x-rays taken on February 21, 2018. Knee x-rays reflected degenerative arthropathy, more pronounced on the left than the right. *Id.* at 14–16, 21–23. A hip x-ray taken on the same day reflected "[e]vidence of some chronic inflammation of the right psoas[59] in insertion upon the lesser trochanter[60] [but] no arthritic changes identified on the right." *Id.* at 17, 24. X-rays of the hands reflected degenerative arthropathy. *Id.* at 18, 25–26. An x-ray of the left foot reflected "[d]emineralization[61] consistent with osteoporosis or osteopenia, but with no complication identified [and] [n]o arthritic changes seen." *Id.* at 19, 27. An x-ray of the right foot reflected "demineralization consistent with osteoporosis or osteopenia [but] [n]o further abnormalit[ies]." *Id.* at 20, 28.

Petitioner also had blood tests on February 21, 2018. Petitioner's 14-3-3η (eta) protein[62] test was high with more than 20 ng/mL, where the reference range is less than 0.2. *Id.* at 29. Petitioner's CCP test had a result of 65 units, indicated as a strong positive. *Id.* Her RF was 153 IU/mL. *Id.* at 31. The modified ESR was 36 mm/hr. C-reactive protein was also high, at 32.4 mg/L, where the reference range is less than 8.0. *Id.* at 32. At the end of the blood tests results, there is a note that the "[b]lood work confirm[ed RA]." *Id.*

3. Petitioner's Testimony

Petitioner testified at the entitlement hearing in this case. *See* Tr. 9:8–54:8. Petitioner explained that she received a flu vaccine every year due to her employment at a hospital, and that she had never had any issues with the vaccine prior to 2013. Tr. 12:14–13:2. She testified that she was "a very healthy and active person," and that she experienced no regular morning stiffness, persistent swelling in her joints, or persistent pain. Tr. 11:9–11, 11:25–12:7. Petitioner testified that she smoked a pack of cigarettes per day for a long time but has since "tried to cut that down because [she] knows it is not good for [her] condition." Tr. 30:12–21.

Petitioner described receiving the vaccine on a Friday evening while at work and testified that she "wasn't feeling quite right" the next day. Tr. 13:16–19. She explained that her symptoms were more "exaggerated" than normal post vaccination symptoms, which she described as "soreness in the injection site" or "aches for a couple of days." Tr. 13:21–22, 28:8–10. Petitioner testified that when she went home after her shift, she could not sleep due to a "deep ache" in her left shoulder, that was "so bad [that she] couldn't sleep and [she] couldn't

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[59] The psoas muscles are defined as "muscles of [the] lower back." They are divided into the psoas minor and psoas major. The former "flexes [the] trunk," while the latter "flexes [the] thigh or trunk." *Dorland's* at 1209, 1547.

[60] Trochanter refers to "either of the two processes below the neck of the femur." *Dorland's* at 1970.

[61] Demineralization refers to "excessive elimination of mineral or inorganic salt[.]" *Dorland's* at 485.

[62] The 14-3-3η (eta) protein "is the newest blood test to be used in the diagnosis of RA. People with RA seem to have elevated levels of the 14-3-3η protein in their blood." *Blood Tests to Help Diagnose Rheumatoid Arthritis (RA)*, ARTHRITIS-HEALTH, https://www.arthritis-health.com/types/rheumatoid/blood-tests-help-diagnose-rheumatoid-arthritis-ra (last visited June 11, 2019).

move literally without helping [her]self turn over." Tr. 14:4–7, 14:14–15. She explained that the pain involved her entire shoulder, not just the site of the vaccination. Tr. 14:6. She testified that she attempted to treat the pain with over the counter medications, but "nothing helped." Tr. 14:16–17.

Petitioner testified that she "joked" with the nurse who administered the vaccine regarding what she perceived to be unusual symptoms. Tr. 13:22–14:3. She explained that she did not report the pain that she was experiencing because she was "not aware at that time" that there was a way to report such a problem. Tr. 29:10–18. Petitioner testified that she is not aware of a way to report issues with the flu vaccine to her employer's workers' compensation provider. Tr. 30:5–11.

Petitioner testified that the pain "subsided somewhat" after approximately three days, and she thought that the problem was resolved. Tr. 14:18. However, three days later the same pain began again in the right shoulder. Tr. 14:21–23. Petitioner stated that the pain was to the point where she was unable to lift her arms above her head to put on a shirt. Tr. 14:23–25. Her shoulders "were red and warm" during this time, and that those symptoms began two to three days after she received the vaccine. Tr. 15:3–4. Petitioner testified that she sometimes required the help of her niece, who would come from about five miles away, to help her get dressed. Tr. 53:1–12.

On November 1, 2013, Petitioner "went to get checked out due to pain in both shoulders." 15:13–20. She testified that it was unusual for her to go to the emergency room, noting that "nobody in healthcare really utilizes the ER unless they really think there is a problem." Tr. 16:2–5. Petitioner's medical record noted that her blood pressure was high due to anxiety related to her pain symptoms. Pet'r's Ex. 3 at 16.

Petitioner described her symptoms between November 1, 2013 and the end of 2013 as "deep, aching" pain. Tr. 16:10–18. She testified that she "never knew where [the pain] was go[ing to] show up," and that it was "sometimes to the point [she] felt [she] couldn't bear it." Tr. 16:19, 16:24. Petitioner explained that she experienced pain in her left knee, then right knee, and that in "one episode [her] hand was very swollen[,] huge and red and hot." Tr. 16:21–23. She testified that the pain "was debilitating and [she] would have to call out of work" when it appeared in her legs. Tr. 16:24–17:1. She testified that she was given a written reprimand at work for absences. Tr. 41:15–23.

Petitioner testified that at her January 2014 MedEx visit several days later, she was unable to walk without a cane due to joint pain. Tr. 18:19–20. She testified that she did not go back to the emergency room because she did not go for routine injury or pain. Tr. 33:1. Petitioner could not recall when she began to use the cane, which belonged to her father, before that visit. Tr. 35:11–20.

Petitioner testified that she continued to have intermittent joint pain between January and April 2014. Tr. 21:11–14. She explained that an ER physician with whom she worked told her that it "sounded as if [she] had something going on that would be best addressed by a rheumatologist," and that the colleague recommended that she visit Dr. Lloyd. Tr. 21:17–21.

Petitioner testified that during her first visit with Dr. Lloyd, he "never touched [her]" and "barely looked at [her]" even though she was "using a cane and crying." Tr. 43:11–15.

Petitioner testified that she saw another rheumatologist on one occasion, but that he was "rude, disrespectful," and "spent most of his time going over the reasons that he would drop [her] as a patient," such as "if [she] was late or missed an appointment." Tr. 44:20–45:3. Petitioner testified that she "never went back because [she] felt that was enough time spent with that doctor." Tr. 45:3–4.

Petitioner testified that prednisone is the "only thing that has kept [her] working." Tr. 19:23–20:1. She testified that she continues to take prednisone "when [she] has flares," but that it "has a lot of side effects." Tr. 25:7–11. Petitioner testified that she continues to have symptoms which she associates with RA, including pain which rises to the point where she uses a wheelchair on occasion. Tr. 25:20–24. She testified that she is scheduled to discuss future treatment options with Dr. Lee at an upcoming appointment. Tr. 26:16–19.

Petitioner testified that none of her treating physicians have opined that the flu vaccine was the cause of her RA. Tr. 44:9–12. She testified that she has discussed the potential connection with Dr. Lee, but that Dr. Lee has not given an opinion either way. Tr. 44:12. Petitioner testified that she submitted a VAERS report because she "felt that [she] had an adverse reaction" to the vaccine. She also contacted an attorney, because she thought "maybe they'[d] heard" about a connection between the flu vaccine and her injuries. Tr. 47:3–4.

III. Expert Review

A. Petitioner's Expert, Dr. Paul J. Utz

Dr. Utz authored three expert reports and testified at the hearing for Petitioner. Pet'r's Exs. 17, 25, 44, ECF Nos. 32-1, 37-1, 55-1. Dr. Utz graduated from Stanford University Medical School in 1991. Pet'r's Ex. 17 at 1. He was board certified in internal medicine from 1994 to 2004 and in rheumatology from 1996 to either 2016 or 2017. *Id.* at 1; Pet'r's Ex. 18 at 1; Tr. 57:1–3. He is a professor of medicine at Stanford University and serves as the Director of Stanford's Medical Scientist Training Program. Pet'r's Ex. 17 at 1. He previously served as Acting Chief of the University of Medicine's Division of Immunology and Rheumatology and as Director of the Center for Clinical Immunology. *Id.* at 2. Dr. Utz has published "probably somewhere between 100 and 150 [publications]." Tr. 59:9–10. That literature does not directly address the causation theory discussed in this case, but it does "include papers on [RA and] autoantibodies." Tr. 59:11–12. He also has experience working with vaccines, as he "was actively involved in vaccine development" with Bayhill Therapeutics for "over a decade" and has "started a new company (Tolerion, Inc in Palo Alto) to pursue vaccine development." Pet'r's Ex. 17 at 1. Dr. Utz testified that he currently runs a research laboratory that studies autoimmune diseases "exclusively [in] humans," although the laboratory "used to also do mouse studies." Tr. 56:4–7.

Since 2010, Dr. Utz has provided expert opinions in nineteen Vaccine Program cases. Pet'r's Ex. 17 at 2. He previously testified twice in the last several years and has authored

approximately twenty reports. Tr. 63:3. He has also reviewed approximately ten to fifteen cases where he has given a preliminary opinion that there was likely no relation between a person's injuries and a vaccine. Tr. 63:8–10. Dr. Utz testified that approximately ten percent of his income derives from litigation, although it varies. Tr. 63:20–21. He testified that he is in the research lab three out of five workdays per week and does administrative work the other two days. Tr. 61:16–21. Dr. Utz stated that his clinical time is inconsistent due to his other responsibilities, but he does volunteer to see patients at the VA hospital, "largely just to cover the other doctors." Tr. 62:2–3. Dr. Utz has treated "hundreds" of patients with RA and recommends they receive vaccines, including the influenza vaccine. Tr. 62:9–22. Respondent had no objection to Dr. Utz's admission as an "expert of medicine in the areas of immunology and rheumatology," and he was so admitted. Tr. 64:11–16.

B. Causation Theory

Dr. Utz opined that, based on Petitioner's "well[]documented history, it is [his] opinion, with a reasonable degree of medical and scientific certainty, that [Petitioner] developed seropositive RA as a direct result of receiving an influenza vaccine." Pet'r's Ex. 17 at 6. He wrote that a review of her medical record "failed to identify any triggering events such as infection or new drug," which left "only her influenza vaccine emerging as the most likely trigger of her disease." *Id.*

Dr. Utz testified that the "etiology of RA is not known," but it is clearly inflammatory and "autoimmune in nature." Tr. 69:23–70:2. He testified that a "variety of different mechanisms" have been discussed in the literature. Tr. 70:5. During his testimony, Dr. Utz stated, "in terms of the mechanism I put forward, molecular mimicry as the primary, although others that could have also been involved included things such as bystander activation of T cells and B cells." Tr. 66:9–12.

Dr. Utz wrote in his first report that "[w]hen an immune response to a non-self-antigen such as components of an influenza vaccine cross reacts with self molecules, the process is termed 'molecular mimicry.'" Pet'r's Ex. 17 at 8. Dr. Utz testified "molecular mimicry is an accepted proposed mechanism in [RA]" that "most rheumatologists would accept." Tr. 71:7–9.

Dr. Utz wrote that "[m]olecular mimicry has been very well[]described in several situations." Pet'r's Ex. 17 at 10. He continued that "[t]he best example" of molecular mimicry "is acute rheumatic fever, in which antigens from beta streptococcus cross react with antigens in the joints, brain, skin and heart, causing acute rheumatic fever." *Id.* Dr. Utz also described "two particularly interesting examples [that] are noteworthy [in the area of vaccines], although there are many others." *Id.* First, Dr. Utz explained that a vaccine was developed for Lyme disease, but was later "withdrawn from the market due to published reports of arthritis induction by the vaccine." *Id.* Dr. Utz wrote that molecular studies demonstrated that arthritis resulted from cross-reactivity between a Lyme protein and a cell surface self-antigen which is critical for immune cells to stick to one other. *Id.* He noted that "[t]he discovery of molecular mimicry caused by the organism itself, and probably also the vaccine, led to [the vaccine's] discontinuation in humans." *Id.* Second, Dr. Utz explained that a vaccine for Hepatitis B was "developed as a conjugate between a hepatitis B antigen and a TLR9 activating DNA

oligonucleotide." *Id.* However, he noted that trials for the vaccine were stopped after two subjects developed an autoimmune condition associated with Hepatitis B, which was thought by the FDA to be related to the vaccine. *Id.*

Dr. Utz opined that "[i]t is plausible, and [he] would argue very likely, that similar molecular mechanisms are at play in [Petitioner's] case." *Id.* The mechanism Dr. Utz proposed is that "influenza antigen(s) in the vaccine are delivered to the immune system, leading to cross[-]reactivity and molecular mimicry to self-antigens that then break tolerance to self, causing RA." *Id.* at 10–11. Dr. Utz elaborated that "[m]any arthritides . . . are postulated to be . . . or known to be . . . caused by exposure to an infectious antigen or foreign antigen." *Id.* at 11. He listed systemic lupus erythematosus[63] ("SLE") and RA as conditions "postulated to be" caused by infectious antigens or foreign antigens, while he listed Lyme arthritis, serum sickness, and parvovirus infection as conditions "known to be" caused by those antigens. *Id.* Dr. Utz wrote that in all of those diseases with a known cause, "ample literature documents that immune complexes can be found early in the disease course[, but] immune complexes may not be present later when patients come to medical attention, suggesting a 'hit-and-run' etiology." *Id.* Dr. Utz opined that RA can be triggered in a similar manner. *Id.*

Dr. Utz wrote that "[i]t is likely in [Petitioner's] case that this is a classic example of a memory immune response in which preexisting memory B and T cells were activated by the vaccine." *Id.* He stated that when compared with primary responses, "memory responses are rapid, and can be orders of magnitude stronger." *Id.* He noted that it is "likely" that "Petitioner would have been exposed to influenza viruses and related antigens during her lifetime." *Id.* Therefore, Dr. Utz explained, "[t]he induction of the cross-reactivity does not require a replicating agent." Tr. 95:5–6. He continued that Petitioner "had a nonreplicating agent, the vaccine, that broke tolerance, even after the vaccine was gone months later, and that was the hit and run event that triggered the immune response." Tr. 95:13–16. Dr. Utz asserted that in this case, Petitioner's arthritis may have been triggered "secondary to formation of immune complexes containing influenza antigens from the vaccine and antibodies produced in response to previous influenza infections or vaccines; activation of T cells from the vaccine; cross-priming to a new antigen; or a combination thereof." Pet'r's Ex. 17 at 11.

Dr. Utz wrote that "[a] number of different RA protein antigens have been described" in the literature, with "the most prominent being Type II collagen, a constituent of joint synovium." *Id.* at 13. He wrote that "[i]njection of Type II collagen in combination with adjuvant into mice leads to the development of B and T cell autoreactivity, associated with severe synovial inflammation (as was observed in [Petitioner] after her vaccination)." *Id.* Dr. Utz stated that Type II collagen is one of the major proteins found in joints and he wrote that "[i]t is well accepted in the field of rheumatology that Type II collagen is an autoantigen in RA." *Id.* at 14. The "collagen molecule, . . . a peptide derived from human collagen, can complex with the HLA-DR4[64] molecule and be presented to lymphocytes." Tr. 98:14–16. Dr. Utz made clear he is not

[63] Systemic lupus erythematosus is "a chronic, inflammatory, often febrile multisystemic disorder of connective tissue that proceeds through remissions and relapses; it may be either acute or insidious in onset and is characterized principally by involvement of the skin, joint, kidneys, and serosal membranes." *Dorland's* at 1080.

[64] Dr. Utz explained in his testimony that HLA-DR4 is a "human leukocyte antigen." Tr. 78:8–10.

stating that "anyone has demonstrated that a T cell receptor is recognizing the collagen and influenza peptides." Tr. 101:18–20. He clarified that "the peptides, when they're in the MHC groove, are structurally similar and, . . . there's a good possibility that collagen peptides and influenza peptides could cross react when they're presented in the context of the DR4 molecule." Tr. 101:22–102:2. Dr. Utz explained by way of analogy. He likened the antigen peptides to hotdogs and the MHC molecule to a hotdog bun. Tr. 77:2–3. He noted that "MHC molecules can see more than one peptide, but not all of them," and an MHC "molecule with the peptide can present that to a T cell, which will then recognize the peptide together with components of [MHC]." *Id.* at 5–9. Under my questioning, Dr. Utz stated that "collagen is by far the antigen where the most evidence exists," but "there could be other antigens besides collagen, including other things that might be citrullinated.[65]" Tr. 358:15–18.

Dr. Utz also referenced an article authored by Sun, et al.,[66] which he wrote "demonstrated that hemagglutinin peptides can activate T cells that can cause synovitis." Pet'r's Ex. 17 at 13 (citing Pet'r's Ex. 17, Ref. 6, ECF No. 32-8). Dr. Utz testified that hemagglutinin, a protein found in the influenza vaccine, "might cross-react or have a similar amino acid sequence [with self-proteins]." Tr. 91:17–21. Dr. Utz stated that several of the articles filed in this case identified peptides present in the influenza vaccine that could cause a cross reactive immune response that triggers RA. Therefore, Dr. Utz concluded that the literature supports his "mechanistic theory that an influenza vaccine constituent can cause RA in a genetically susceptible individual." Pet'r's Ex. 17 at 14.

Dr. Utz acknowledged that he found "no epidemiologic link between RA and influenza vaccination" in the literature that he searched but stated that it was unsurprising that he found no such link,[67] and that such a link is not required to support his theory. *Id.* at 11.

C. Petitioner's Diagnosis and Current Health

Dr. Utz reviewed and summarized Petitioner's medical history and affidavit in his reports and again during his testimony. Pet'r's Ex. 17 at 2–6; Tr. 55–216. He explained that RA is an autoimmune disease that can be diagnosed following an examination of the patient's joints and laboratory testing, including tests for RF and CCP. Tr. 69:9–20. He opined that Petitioner "had no preexisting evidence that she had any systemic rheumatic disease or any arthralgia or other joint problems that would have predisposed her to [RA] . . . ." Tr. 65:19–22. Dr. Utz did note that Petitioner "had an important risk factor (tobacco use) that is strongly believed to play an additional role in the development of CCP-positive RA." Pet'r's Ex. 17 at 7. In his report, Dr. Utz wrote that although "smoking is believed to be an environmental contributor to the development of RA[, it] is not associated with acute triggering of rheumatic disease as has been

[65] Citrullination is "a posttranslational modification of proteins in which peptideylarginine deiminase catalyzes the conversion of arginine residues to citrulline residues. . . . [I]t also occurs in a variety of inflammatory conditions." *Dorland's* at 366.

[66] Jian Sun et al., *Superior Molecularly Altered Influenza Virus Hemagglutinin Peptide 308–317 Inhibits Collagen-Induced Arthritis by Inducing CD4+ Treg Cell Expansion*, ARTHRITIS & RHEUMATOLOGY (2012) 64:2158–68.

[67] Dr. Utz noted that "even large epidemiologic studies will not have the power to capture rare, patient-specific events such as occurred in [Petitioner's] case." Pet'r's Ex. 17 at 12.

overserved with vaccines, certain drugs, and infections." *Id.* at 6–7. Dr. Utz later wrote that "Petitioner has a genetic predisposition to develop RA and that tobacco use over 40 years increased her likelihood of developing seropositive RA if she encountered the 'right', or in this case 'wrong/bad', environmental trigger." Pet'r's Ex. 25 at 3. He followed that assertion with testimony that Petitioner "was probably DR4 positive. We don't know that for sure." Tr. 137:7–8.

Dr. Utz noted in his report that there are researchers that have studied "a 'preclinical' period of disease" that "is characterized by abnormalities in disease-related biomarkers before the onset of the clinically apparent signs and symptoms." *See* Pet'r's Ex. 25 at 4–7 (citing Resp't's Ex. Q[68] at 1–4). Dr. Utz wrote that this research is developed with the hope that biomarkers of autoimmunity present during this period can be used to reverse or prevent tissue damage and the future development of clinically apparent disease, and is not focused on identifying potential triggers for the development of RA. Dr. Utz asserted that the categorization of an individual as preclinical is controversial because all individuals who exhibit these biomarkers do not always go on to develop RA. In fact, one of these researchers, Dr. Kevin Deane, noted that "we don't know . . . what drives the initial development of autoantibodies . . . what triggers the expansion of autoimmunity . . . or what leads to the transition . . . to clinically apparent synovitis." Pet'r's Ex. 25 at 4 (citing Resp't's Ex. C at 7 (citing Resp't's Ex. R[69] at 1.)) Dr. Utz cautioned against designation of a patient as preclinical because the authors themselves stated "this relationship has largely been studied retrospectively in patients with established disease [and] whether smoking is an initial trigger for autoimmunity . . . remains unclear." Pet'r's Ex. 25 at 6 (citing Resp't's Ex. Q at 3).

In his report, Dr. Utz relied on Petitioner's statements to identify the onset of her symptoms. He noted that "[a]ccording to [Petitioner's] affidavit, on October 20, 2013, [one day post vaccination, Petitioner's] left shoulder was sore." *Id.* at 3. Dr. Utz later wrote in his report that "Petitioner developed severe pain in the shoulders and other joints within hours to days of vaccination, followed by polyarticular arthralgia and ultimately inflammatory arthritis." *Id.* at 15. During his testimony, Dr. Utz stated that "[he] now think[s] more about three to six days were more around the time where–she was really struggling the first three days, but then the three to six days." Tr. 65:25–66:3.

Dr. Utz highlighted that Petitioner "was negative for RF and [CCP] soon after vaccination, but then went on to develop positive tests for both factors over time." Pet'r's Ex. 17 at 7. Dr. Utz noted that RA onset can be acute or subacute, as in Petitioner's case. *Id.* at 11. Dr. Utz testified that Petitioner detailed symptoms within days after the vaccination that were very compelling, such as her inability to dress herself. Tr. 53:1–5; Tr. 197:9. He testified that based on her account, "the trigger for her RA was the vaccine" within three to six days. Tr. 138:10.

Dr. Utz wrote that Petitioner's "ongoing treatment with moderately high doses of corticosteroids very likely contributed to her stuttering course and delay in meeting

[68] Kevin D. Deane & Hani El-Gabalawy, *Pathogenesis and Prevention of Rheumatic Disease: Focus on Preclinical RA and SLE*, NAT. REV. RHEUMATOL. (2014) 10:212–28.
[69] Kevin D. Deane, *Autoantibodies, Citrullinated Histones and Initiation of Synovitis*, NATURE REV. RHEUMATOLOGY (2015) 11:688–89.

Classification Criteria for [RA]." Pet'r's Ex. 17 at 7. Dr. Utz wrote that Petitioner currently meets the criteria for the diagnosis of RA. *Id.*

D. Respondent's Expert, Dr. Mehrdad Matloubian

Dr. Matloubian authored two expert reports and testified at the hearing on behalf of Respondent. Resp't's Exs. C, UU, ECF Nos. 34-1, 62-1; Tr. 224–337. Dr. Matloubian graduated from the University of California, Los Angeles School of Medicine in 1996. Resp't's Ex. D at 2, ECF No. 34-2. While in medical school, Dr. Matloubian also received a Ph.D. in virology in the Department of Microbiology and Immunology. *Id.* Dr. Matloubian is currently board certified in rheumatology and was previously certified in internal medicine. Tr. 225:16–18. Dr. Matloubian is an associate professor at the University of California, San Francisco School of Medicine, Rheumatology Division. Tr. 225:21–23. Dr. Matloubian's other roles at the University of California, San Francisco include Director of the Rheumatology Precision Medicine Corps. and Co-Director of the Molecular Medicine Consult Service. Tr. 226:9–10, 22–23.

Dr. Matloubian has engaged in virology- and immunology-based research for over twenty years. Resp't's Ex. C at 2. He has published peer-reviewed articles focused on "innate and adaptive immune responses, including those of T and B cells, to acute and chronic viral infections." *Id.* In addition to teaching, Dr. Matloubian is a practicing rheumatologist and sees patients once a week. Tr. 228:2–3. He treats patients with autoimmune rheumatologic diseases, including RA, and he has diagnosed patients with RA. Tr. 228:16–229:8. Dr. Matloubian testified that he has seen approximately one hundred RA patients in a given year. Tr. 229:14–15. He has appeared as an expert witness for Respondent approximately thirty times and testified at hearing seven times beginning in 2015. Tr. 231:17–24. Dr. Matloubian stated that about fifteen percent of his annual income comes from his participation in the program. Tr. 232:5. Dr. Matloubian was admitted to testify as an expert in rheumatology and immunology with no objection from Petitioner.

E. Dr. Matloubian's Reports and Testimony

Dr. Matloubian began his expert report with a recount of Petitioner's medical history. Resp't's Ex. C at 1–4. The report identifies two major questions with respect to Petitioner's case: "1) What is the rheumatologic diagnosis for the [P]etitioner's musculoskeletal complaints; and 2) Was her condition caused by her influenza vaccination?" *Id.* at 4.

Dr. Matloubian did not dispute that Petitioner suffers from RA. Dr. Matloubian agreed that the "diagnosis of seropositive RA is quite reasonable in [Petitioner's] case." *Id.* at 5. He also agreed "with Dr. Vazquez[] . . . that a chronic pain syndrome influence by [P]etitioner's history of anxiety and depression as well as osteoarthritis of her knees . . . were most likely contributing to her musculoskeletal symptomatology." *Id.*

Dr. Matloubian described RA as "a systemic inflammatory disease whose major manifestation is peripheral arthritis, mainly in the small joints of the hands and feet." *Id.* Dr. Matloubian noted that RA is "quite common," particularly "between the ages of 50 and 75." *Id.* He added that about one percent of the Caucasian population is affected and there is a "lifetime risk of . . . 3.6% (1 in 29) for women." *Id.* Dr. Matloubian described presentations of RA ranging from "fulminant" to "insidious" and detailed an "established [] set of validated criteria" for diagnosis. *Id.* These criteria include the number and site of involved joints with synovitis and serological abnormalities. *Id.* During his testimony, Dr. Matloubian distinguished between seronegative and seropositive RA, stating that the latter, "which is about two-thirds of the cases, is characterized by having either anti-CCP antibodies or [RF] or both." Tr. 233:1–3.

Dr. Matloubian explained that "autoantibodies that are specific for [RA] are directed against [] citrullinated protein epitopes," but "[RF] has an unfortunate name because it is not unique to [RA] and occurs in many other diseases . . . [involving] chronic stimulation of the immune system." Tr. 235:22–25. Dr. Matloubian also cautioned that "when patients present with [RA] clinically, [e.g.,] with joint inflammation[,] . . . the disease actually started years before and what supports that is that many of the patients have positive anti-CCP antibodies . . ." Tr. 236:13–16. He stated this chronology "is not something that is disputed in the rheumatology community, and there is a lot of effort to identify the different stages of preclinical [RA]." Tr. 236:22–24.

Dr. Matloubian wrote in his report that "[t]he pathogenesis of RA is quite complex and not completely understood." Resp't's Ex. C at 4. Dr. Matloubian's report also included Figure 2 taken from the van Steenbergen et al.[70] article illustrating the "six phases of RA development." *Id.* at 6 (citing Resp't's Ex. O at 2221). The figure is comprised of six stick figures that correspond to each phase and help to explain the progression of the disease. *Id.* Dr. Matloubian also used this figure during his testimony. Tr. 237:7–239:9. Phases A and B highlight the impact of genetic factors, such as HLA-DRB1 shared epitope, and environmental factors, such as smoking and antibiotics. Resp't's Ex. C at 6. Dr. Matloubian stated that "about 50 percent of the risk for RA comes from the genes, and half of that comes from the HLA-DR4 that Dr. Utz discussed." Tr. 237:14–15. Dr. Matloubian continued to explain that phase B is "a person who has a genetic risk, and then they get exposed to an environmental risk factor . . . –the major risk factor [being] smoking." Tr. 237:17–20. Ultimately the genetics and the environment "lead[] to the production of anti-CCP antibodies, and this [is] phase C." Tr. 237:24–25. Dr. Matloubian noted that the illustration for phase C in the figure is shaped like an antibody to denote autoimmunity and to underscore that this phase is "defined by breakdown of tolerance to self-antigens[that] happens when a person becomes anti-CCP positive." Tr. 238:2–4. The remaining phases D, E, and F illustrate the development of clinical symptoms that are then categorized first as generalized symptoms, then undifferentiated arthritis, and ultimately diagnosed as RA with the onset of joint inflammation. Resp't's Ex. C at 6. Dr. Matloubian noted during his testimony

[70] H.W. van Steenbergen et al., *The Preclinical Phase of Rheumatoid Arthritis: What is Acknowledged and What Needs to be Assessed?*, ARTHRITIS RHEUMATISM 65(9):2219–32 (2013).

that it is unknown "how long it will take an individual to go from development of anti-CCP to development of [RA], and not everybody goes through all phases." Tr. 239:5–8. Dr. Matloubian cited the Deane papers to assert that despite the largely unknown pathogenesis of RA, "[e]stablished and emerging data demonstrate that [there is] a preclinical period." Resp't's Ex. Q at 1. He continued that "[n]umerous genetic and environmental risk factors for [autoimmune rheumatoid diseases] have also been identified, and many of these factors are likely to act before the clinical appearance of tissue injury to initiate and/or propagate autoimmunity and autoimmune disease." *Id.* In his report, Dr. Matloubian also stated that there is a "lag of many years" between autoantibody development and clinical symptoms of RA. Resp't's Ex. C at 7. And, because of this delay, "it is extremely difficult to establish a causal link to a specific environmental exposure, and one cannot completely rule out stochastic (e.g., random) immunologic events." *Id.*

Dr. Matloubian was asked how the phases of RA development applied in Petitioner's case. Dr. Matloubian stated that prior to Petitioner's vaccination in October 2013, Petitioner did not suffer from stiffness, persistent swelling or pain, or inflammatory arthritis. Tr. 314:2–8. Dr. Matloubian wrote in his report that "[P]etitioner did not have either a personal history or a family history of autoimmune diseases, suggesting unlikelihood of a genetic predisposition." Resp't's Ex. C at 9. He testified that, at the time of the vaccination, Petitioner had environmental risk factors for several years and, "[b]ased on what we know about the natural history of [RA] . . . [Petitioner] was most likely in Phase C, because there's a strong link between smoking, genetics, and development of anti-CCP." Tr. 321:7–11. He noted that he could not find where Petitioner suffered from joint pain in her knuckles or her feet and stated that he was "not sure she even went through Phase D." Tr. 321:17–24. Dr. Matloubian identified Petitioner's "swollen, red, hot knee" treated on April 3, 2014 as the first evidence of her inflammatory arthritis and asserted that "chances were high that [Petitioner] was anti-CCP positive before she developed her inflammatory arthritis." Tr. 314:17–19. These symptoms, Dr. Matloubian argued, were evidence of Phase E. Tr. 322:23. Dr. Matloubian stated that Petitioner was into Phase F when she presented to Dr. Lloyd with inflammation of the small joints and hands on April 27, 2014. Tr. 323:9–18. He noted that Petitioner's blood test that identified the presence of anti-CCP occurred at her April 16, 2014 visit. Tr. 323:24–25.

Dr. Matloubian was then asked how these phases can be applied to any specific patient if phases can be experienced out of order or skipped altogether. He stated the figure illustrates "proposed preclinical phases" to "identify people and put in an intervention." Tr. 335:8, 23–24. He clarified that the point of the paper is to help the Court understand and not necessarily to apply each phase to Petitioner's case. Tr. 334:16–20. Although each patient can proceed through the phases differently, Dr. Matloubian testified that he is "not aware that somebody [could] present[] with . . . symmetric arthritis and then develop [RF], [despite the fact that] most people, at the time of diagnosis, are anti-CCP positive." Tr. 336:14–17. Dr. Matloubian could not see how the clinical presentation could appear prior to the development of RF. Tr. 336:12–17.

Dr. Matloubian then turned to whether Petitioner's condition was caused by the flu vaccine. In his report, he concluded that "[P]etitioner's major risk factor for development of RA is her long history of smoking." Resp't's Ex. C at 7. Dr. Matloubian also concluded that "[P]etitioner had most likely developed positive anti-CCP antibodies years before her presentation with inflammatory arthritis, and thus had a silent autoimmune disease." *Id.* To determine whether vaccination can act as a trigger for symptoms of RA and cause a patient to move from phase C to phase D in the progression, Dr. Matloubian returned to a discussion of the filed literature. His report cited to Ray et. al.,[71] a small case-control study, and Bengtsson et. al.,[72] a "much larger and more extensive study. *Id.* The authors of the smaller study "did not find any association between influenza vaccination and development of RA." *Id.* The authors of the larger study found "vaccinations neither increased the risk of RA overall nor the risk of two major subgroups of RA [CCP positive or negative] . . . . Furthermore, vaccinations did not increase the risk of RA in smokers or carriers of HLA-DRBi shared epitope alleles, two groups with established risk factors for RA." *Id.* Dr. Matloubian noted in his report one article[73] that stated case reports and case series suggest a link between RA and vaccination, but the authors cautioned that "establishing a causal association requires a comparative group who have not been immunized." *Id.* at 8 (quoting Resp't's Ex. W at 2).

Dr. Matloubian also discussed three arguments from the Schattner study[74] to rebut Dr. Utz. Resp't's Ex. C at 8 (citing Resp't's Ex. X at 3881). "First, [specific] virus infections should be linked to [specific] autoimmunity. Second, a mechanism or mechanisms whereby exposure to viral antigens (be it during infection or vaccination) lead to autoimmunity must be established. Third, evidence must be obtained that patients who have been vaccinated against specific viruses developed a specific autoimmune disease, bearing in mind that association alone does not necessarily indicate causality." *Id.* (emphasis in original).

Dr. Matloubian testified that it is significant that RA patients are still encouraged to get flu vaccines. Tr. 288:1. He explained that "people who have [RA] are generally on immunosuppressive medication, so if they get the actual [flu] infection, they have a higher risk of having really bad outcomes." Tr. 288:5–8. Dr. Matloubian concluded that "the rheumatology community and the medical community [do] not think that influenza vaccine is a risk for RA patients." Tr. 288:11–13.

During his testimony, Dr. Matloubian also opined that "most autoimmune diseases are not associated with infections." Tr. 255:1–2. He explained that some autoimmune diseases are

[71] Paula Ray et al., *Risk of Rheumatoid Arthritis Following Vaccination with Tetanus, Influenza, and Hepatitis B Vaccines Among Persons 15–59 Years of Age*, VACCINE 29:6592–97 (2011).
[72] Camilla Bengtsson et al., *Common Vaccinations Among Adults Do Not Increase the Risk of Developing Rheumatoid Arthritis: Results From the Swedish EIRA Study*, ANN. RHEUM. DIS. 69:1831–33 (2010).
[73] D.P.M. Symmons & K. Chakravarty, *Can Immunization Trigger Rheumatoid Arthritis?*, ANNALS OF THE RHEUMATIC DISEASES 52:843–44 (1993).
[74] Ami Schattner, *Consequence or Coincidence? The Occurrence, Pathogenesis and Significance of Autoimmune Manifestations After Viral Vaccines*, VACCINE 23:3879–86 (2005).

"single-gene mutation" diseases that do not need a trigger and "tend to happen earlier in life." Tr. 255:3–5. He also provided examples of autoimmune diseases "associated with infection, such as psoriasis." Tr. 255:6–7. RA is not considered to be a post infectious disease, although Dr. Matloubian clarified that there is such a thing as post infectious inflammatory arthritis. Tr. 255:20–256:1. He testified that these "disappear after two-four weeks, and they don't go on to become autoimmune arthritis . . . in the most part." Tr. 256:12–14.

Dr. Matloubian discussed case reports of RA following an influenza vaccination. He stated that the relationship is entirely based on timing. "They don't really talk about causation or mechanistic relationships." Tr. 292:14–15. Dr. Matloubian strongly objected to Dr. Utz's molecular mimicry causation theory. He conceded that molecular mimicry has been established as mechanism for other autoimmune diseases such as "rheumatic fever happening after Group A streptococcus infection and for Guillain-Barré, happening after campylobacter jejuni." Tr. 258:21–23. In both those cases, Dr. Matloubian explained, "the same T cells see the pathogen-specific peptide and the self-peptide, then that T cell is called cross-reactive, because it can cross-react between those two, and that's the basis of molecular mimicry is that the T cell sees them as the same." Tr. 259:21–25. Dr. Matloubian emphasized that it is not enough for the T cell to see them both; the T cell must see them as the same thing. Tr. 260:7–22. He stated there have been many examples of "sequence homology, but when they test it out, it do[es not] pan out as either activating the T cells being cross-reactive or causing disease." Tr. 260:18–20.

Dr. Matloubian described Dr. Utz's theory of "molecular mimicry between the influenza hemagglutinin, or HA and collagen, which is an antigen in [RA], [stating] the vaccine-activated influenza-specific T cells, [] then cross reacted with self-collagen and caused, allegedly, [RA]." Tr. 266:25–267:4. Dr. Matloubian identified this as an oversimplification of molecular mimicry and testified about the "Characteristics of Peptide-MHC Molecule Interactions"[75] to describe "how a peptide binds to an MHC or HLA molecule." Tr. 268:21–23. Dr. Matloubian testified that "each of us have six MHCs, and they're different from each other." Tr. 269:16–17. He explained that when an individual is infected with influenza, MHCs will present peptides derived from the pathogen so they can bind to them. Every person's immune system creates their own peptides, and although "the peptides that bind to MHC molecules share structural features that promote this interaction," each person has different peptides created by that person's immune system. Tr. 270:3–5. Furthermore, "[t]he residues of a peptide that bind to the MHC molecules are distinct from those recognized by T cells." Tr. 270:15–16. Ultimately, Dr. Matloubian explained that "the peptide has these anchor residues that fit in the pocket of MHC." Tr. 271:1–2. He continued, "they bind to the MHC, but what the T cell sees . . . is on top of the peptide and very different from the contact residues that allow the peptide to bind to the MHC." Tr. 271:2–5.

Using Dr. Utz's analogy, Dr. Matloubian stated that all the peptides have the same hotdog structure to sit in the MHC molecule bun, but the T cells only care about what condiments are on the hot dog and not the hotdog or the bun. Tr. 272:10–17. Dr. Matloubian

[75] A.K. ABBAS ET AL., *Chapter 6: Antigen Presentation to T Lymphocytes and the Functions of Major Histocompatibility Complex Molecules*, in CELLULAR AND MOLECULAR IMMUNOLOGY (9th ed. 2018).

criticized the literature that Dr. Utz filed stating there are no data to suggest "that just because the peptides have the same conformation, meaning that they bind, they fit in that peptide groove, that means that the same T cell receptor can see them both." Tr. 277:20–24. Dr. Matloubian asserted that "in vitro phenomena do[ ] not necessarily translate to causing a disease in a human." Tr. 261:24–25. He continued, that cross-reacting antibodies in tissue culture does not mean that inside the body those cells "cause tissue damage and cause disease." Tr. 262:4–6. Dr. Matloubian concluded that "[t]he only thing that Dr. Utz showed in those papers is that collagen and hemagglutinin [ ] can bind to DR4, and that by itself doesn't mean that the same T cell receptor can see both antigens." Tr. 273:7–11

Dr. Matloubian admitted on cross-examination that other individuals who are considered experts in this field have hypothesized that molecular mimicry could be the basis of a causal relationship between infectious agents and RA. Tr. 304:20.

Dr. Matloubian was also asked about his assertion that Petitioner did not exhibit any evidence of inflammatory arthritis prior to her swollen knee. Tr. 315:12–13. He conceded that she complained of swelling in her extremities but categorized the complaint as an isolated wrist injury attributed to acute trauma. Tr. 316:3–6. When asked whether the prednisone treatment is evidence that her treater was concerned about inflammation, Dr. Matloubian stated, "whoever is prescribing it thought that the person must have had inflammation at one point." Tr. 318:6–8.

IV. The Applicable Legal Standard

To receive compensation under the Vaccine Act, Petitioner must demonstrate either that: (1) she suffered a "Table Injury" – i.e., an injury falling within the Vaccine Injury Table – corresponding to the vaccine in question within the time frame prescribed by the Vaccine Injury Table set forth at § 14, as amended by 42 C.F.R. § 100.3; or (2) that her illness is an "off-Table Injury," one not listed on the Table, that resulted from her receipt of a covered vaccine. *See* § 11(c)(1)(C); *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner does not assert a Table claim. Thus, it must be proven that her vaccine was the cause-in-fact of her injury.

To establish causation-in-fact, Petitioner must demonstrate by a preponderance of the evidence that the vaccines were the cause of her injury. § 13(a)(1)(A). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioner must demonstrate that the vaccine was "'not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury.'" *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)). The vaccine received, however, need not be the predominant cause of the injury. *Shyface*, 165 F.3d at 1351.

A petitioner may not receive a Vaccine Program award based solely on her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1). In *Althen v. Sec'y of Health & Human Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278 (Fed. Cir. 2005). The *Althen* test requires a petitioner to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id.* (internal citations omitted).

Specifically, under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question "can [the] vaccine(s) at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *aff'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). This may be accomplished in a number of ways. "Reliability and plausibility of . . . pathogenesis can be bolstered by providing evidence that at least a sufficient minority in the medical community has accepted the theory, so as to render it credible." *Id.* Additionally, "epidemiological studies and an expert's experience, while not dispositive, lend significant credence to the claim of plausibility." *Id.* Medical literature published in respected medical journals is also persuasive. *Id.* "However, publication 'does *not* necessarily correlate with reliability,' because 'in some instances well-grounded but innovative theories will not have been published.'" *Id.* (quoting *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 593–94 (1993) (emphasis in original)). Furthermore, a petitioner is not required to present medical literature or epidemiological studies to prove her burden. *Grant v. Sec'y of Health and Human Servs.*, 956 F.2d 1144, 1149 (Fed. Cir. 1992); *Andreu v. Sec'y Health & Human Servs.*, 569 F.3d 1367, 1380 (Fed. Cir. 2009). However, to the extent medical literature and epidemiological studies are provided, these are subject to critique by Respondent's experts, and the special master will consider them when deciding whether the petitioner has met her burden of proof. Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. But this does not negate or reduce a petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).

In addition to showing that the vaccine at issue can cause a particular injury, a petitioner must also, under *Althen's* second prong, prove that the vaccine actually did cause the alleged injury in her particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1278. A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original) (internal citations omitted). Ruling out other potential causes is an important element but does not itself establish causation. *Id.* Additionally, conjecture or speculation does not meet the preponderance standard. *Id.*

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Human Servs.*, 24 Cl. Ct. 400, 403–04 (Fed. Cl. Oct. 23, 1991); *see also Grant*, 956 F.2d at 1148 ("'[T]he inoculation is not the cause of every event that occurs within the ten[-]day period. . . . Without more, this proximate temporal relationship will not support a finding of causation.'" (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))). A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (Althen prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), aff'd mem., 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Petitioners who demonstrate by a preponderance of the evidence that they suffered an injury caused by vaccination are entitled to compensation, unless Respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Paluck v. Sec'y of Health & Human Servs.*, 786 F.3d 1373, 1386 (Fed. Cir. 2015) (citing *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008) (holding that it is not a petitioner's burden "to rule out possible alternative causes" (internal citations omitted))); *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994).

Respondent frequently offers experts to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (internal citations omitted). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Both parties filed medical and scientific literature in this case, but not every filed item was probative to the outcome of this decision. While I have reviewed all of the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case – just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record

evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to – and likely undermines – the conclusion that it was not considered").

V. Analysis

A. Experts

Petitioner's expert Dr. Utz and Respondent's expert Dr. Matloubian both have a background in rheumatology. Dr. Utz was board certified for many years up until recently, whereas Dr. Matloubian maintains his certification. Although Dr. Utz does not regularly see patients, it is clear from his testimony that he is well versed in the symptomology and diagnostics of RA.

Drs. Utz and Matloubian were also admitted as experts in immunology due to work each has done in academic and research settings. Dr. Utz articulated a molecular mimicry causation theory. His work in vaccine development qualifies him to assert such a theory. Dr. Matloubian's research on the innate and adaptive responses of the immune system to acute and chronic infections provides credibility to his criticisms of Dr. Utz's theory. Despite their uncontested qualifications, there is little that the experts agree on outside of Petitioner's ultimate diagnosis.

B. *Althen* prong one

In his report, Dr. Utz initially identified several different mechanisms, one or more of which could be a contributor to his proposed causation theory. This is problematic because to satisfy prong two of *Althen*, there must be a medical theory presented that can be applied to Petitioner's case to show a logical sequence of cause and effect between Petitioner's vaccination and injury. Practically, it is difficult to apply a theory to a fact pattern if the theory is non-specific. Dr. Utz wrote that Petitioner's injury may have occurred "through molecular mimicry, formation of immune complexes, cross-priming, or a combination of these." Pet'r's Ex. 17 at 14. Dr. Utz testified that molecular mimicry was the primary mechanism that he put forward, although he added that "others that could have also been involved included things such as bystander activation of T cells and B cells." Tr. 66:9–12. Alternatives notwithstanding, Dr. Utz focused almost exclusively on molecular mimicry in his writings and testimony. Consequently, that was also the focus of Dr. Matloubian's response. Dr. Utz did not explain how any of these additional mechanisms could combine with molecular mimicry in a case involving the flu vaccine and RA. He also did not explain how it would be possible to determine which, if any, of these various mechanisms would be applicable to Petitioner's case. Dr. Utz's inability to unequivocally identify his theory of causation (with or without identifying the specifics of the mechanism) undercuts his assertation that his opinion meets the more likely than not standard. This kitchen-sink approach is overbroad and vague. Because of the lack of evidence provided with respect to the other theories, I find that there has not been persuasive evidence to support any of them by a more likely than not standard. Therefore, I will focus solely on his theory of molecular mimicry.

Drs. Utz and Matloubian agreed that RA is an autoimmune, anti-inflammatory disease. They also agreed that molecular mimicry can be a reliable causation theory for some autoimmune diseases. They disagree whether RA could have a molecular mimicry pathogenesis if the etiology is not infectious. Dr. Utz never directly addressed whether he believes a disease has to be post infectious for molecular mimicry to apply. He did, however, state in his supplemental report that he has "taken the position repeatedly, in all non-adjuvanted vaccine cases in which [he] ha[s] served as an expert, that molecular mimicry is a valid hypothesis, noting that [it] cannot be proven in humans." Pet'r's Ex. 44 at 6. This suggests that the etiology of a condition is irrelevant to his assessment of whether molecular mimicry can apply. Dr. Utz asserted that in RA cases, a susceptible individual can be triggered by the immune system's repeated exposure to certain influenza peptides, whether from the wild virus or vaccinations. He does not clarify if exposure to the wild virus is needed, or if multiple vaccinations will suffice. This argument implies that RA could be post infectious, because the HA peptide at the heart of his theory is present in the virus and the vaccine. It is unclear how Dr. Utz would articulate his molecular mimicry theory in a case that clearly involves a non-infectious disease, but that question need not be answered here. Dr. Utz argued that in a case such as Petitioner's, vaccination could cause the immune response necessary to trigger autoimmunity without infection because most adults have been exposed previously to the flu several times through prior vaccinations or infection. Dr. Matloubian was more definitive. He testified that molecular mimicry is "not necessarily an explanation for all kinds of autoimmune disease, especially those that are not associated with infection." Tr. 259:8–10. Furthermore, Dr. Matloubian testified that RA is not post infectious, and the flu virus has not been identified as a trigger for RA. Dr. Matloubian asserted that Dr. Utz could not provide any literature that RA has been linked to influenza, however, there is evidence that other rheumatological conditions and autoimmune diseases have been linked, in rare cases, to influenza. Dr. Matloubian embraced this evidence to argue that these same links should be seen in RA cases but are not. Dr. Matloubian wrote, "[t]he fact that development of an autoimmune inflammatory arthritis after an influenza infection has not been described strongly argues against Dr. Utz's molecular mimicry theory," particularly when this same condition "has been described to occur after much rarer viral infections, such as Chikungunya virus." Resp't's Ex. UU at 8.

Dr. Matloubian is correct that Petitioner has not presented any publications to support his contention. However, in the vaccine program, the lack of studies is not probative evidence that a theory should be discounted. This is largely due to the rare nature of most of the alleged vaccine injuries and the improbability or impossibility that properly controlled studies could be conducted. Dr. Matloubian's reliance on the Chikungunya virus does identify an instance wherein the actual increase in the occurrence of such a rare disease generates statistical abnormalities sufficient to infer causation. However, RA is not quite as rare. In cases where the alleged condition is rare, but not unheard of, a small absolute increase in the number of patients may not generate a statistically significant percentage increase for researches. This does not disprove causation for the rare case.

Furthermore, Respondent has provided no study that definitively disproves Dr. Utz's assertion. There have been some large-scale studies that resulted from researchers and experts identifying multiple case reports linking a particular vaccine to a type of illness. These studies

have been used to establish causation in some cases and negate it in others. Dr. Matloubian conceded that the flu vaccine has been causally linked to other autoimmune diseases and arthralgias. Tr. 258:21–23; Tr. 306:11. He also noted that case reports have linked inflammatory arthritis to the flu. Tr. 308:16–18. Dr. Matloubian went further on cross-examination, "[activation of the immune system through vaccination] was postulated as a mechanism, a risk factor in contributing to – on top of the other risk factors to RA . . ." Tr. 305:23–306:8. Dr. Utz has identified molecular mimicry as a potential mechanism for the flu vaccine to cause RA that has been considered in the field, but not sufficiently tested for the literature to be dispositive.

The experts agreed that RA patients should be vaccinated against the flu, and Dr. Matloubian argued that this is further evidence that the vaccine is not a factor in the development or progression of RA. The recommendation that RA patients are vaccinated is also consistent with the Bengtsson et al. study's conclusions that "it is unlikely that vaccinations in general should be considered as a major risk factor for RA" and "active immunisation does not increase the risk of RA in individuals with major risk factors." Resp't's Ex. C at 9; Resp't's Ex. B at 5. Although the lack of corroborative studies cannot be the basis to discount a proposed theory, Respondent has relied on a persuasive study that shows the greater rheumatology community found no increased risk for development of RA in individuals with risk factors post vaccination. That does not mean, however, that Petitioner's theory could not occur in a given case. Vaccine-caused injuries are rare by definition, and usually the exception to the rule.

Respondent's main argument attacks the specific peptides that Dr. Utz identified for cross-reactivity. In the spirit of the program, "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program." *Knudsen*, 35 F.3d at 549. Petitioners are tasked, however, with presenting a "sequence of cause and effect [that] is logical and legally probable." *Id.* at 548–59. In other words, to the extent that petitioners do present a specific biological mechanism, it must make sense. Other cases in the program where petitioners' expert unsuccessfully identified the relevant proteins and affected body systems have failed because the disease pathogenesis was not consistent with the identified immune response. *See Jewell v. Sec'y of Health and Human Servs.*, No. 11-138V, 2016 WL 5404165 (Fed. Cl. Spec. Mstr. Aug. 29, 2015) (petitioners failed to prove that cytokine activity is capable of impacting the brain's 5-HT system in the ways proposed by petitioners' experts); *see also Dougherty v. Sec'y of Health and Human Servs.*, No. 15-1333V, 2018 WL 3989519 (Fed. Cl. Spec. Mstr. July 5, 2018) (petitioner failed to provide evidence that antibodies reacting to hypocretin-2 receptors would only damage these receptors if located in a limited region in the brain, despite their widespread presence in other regions of the body).

In the present case, Dr. Utz identified a specific viral antigen that is present in the flu vaccine, HA, and explained how it can bind to DR4. He then identified the human autoantigen collagen that can also bind to DR4 with a similar structure to HA. Dr. Matloubian agreed that both peptides bind to DR4 but did not agree that cross-reactivity would occur or that disease would be the result. Drs. Utz and Matloubian both explained how the T cell receptors reacted to peptides with similar homology. Dr. Utz provided literature in an attempt to show that despite an inability to definitively prove it, other experts believed the similarity between the two peptides

suggested that the peptide found in the vaccine could be misinterpreted as the autoantigen found in RA patients. Dr. Matloubian countered that Dr. Utz's theory is improbable without evidence "that the T cells that can cause [RA] can recognize **and be activated** by both antigen that is derived from that vaccine, as well as antigens that are . . . related to that disease." Tr. 309:5–7 (emphasis added). Dr. Matloubian stated that one of the papers Dr. Utz relied on undercut his theory because the authors found "when HA binds to HLA-DR4, because of the interactions with it, the whole molecule looks different than when collagen binds to HLA-DR4." Tr. 275:15–17.

Dr. Utz's assertion that this cross-reaction occurs and induces RA has not been established by medical literature, but again, that is not the standard in the vaccine program. The difficulty in determining the viability of a theory that is novel or rarely applicable highlights the unknown etiology of many conditions seen in the program. Dr. Utz has been able to identify a peptide that is an autoantigen in RA and similar in composition to another peptide that is found in the flu virus and vaccine. Because of his specificity, it is possible to better understand that the respective roles of these peptides during immune system response and in the pathogenesis of RA are consistent with cross-reactivation. Whether Dr. Utz's theory is applicable to Petitioner's case turns on his assertions that: (1) she was not preclinical, (2) vaccination is a necessary trigger, and (3) the timeframe for symptom onset was appropriate. That analysis will be done pursuant to prong two. Generally, Dr. Utz has presented a theory that explains how seropositive RA could develop in an individual with environmental and genetic risk factors, who was otherwise asymptomatic.

It should be noted that Petitioner did not submit a significant aggravation claim in this case. Dr. Utz did not argue that Petitioner's vaccination hastened her development of RA. In fact, Dr. Utz took issue with Dr. Matloubian's assertion that Petitioner suffered from preclinical RA. He stated, "[i]t is misleading to think that all asymptomatic individuals with abnormal cytokines levels or positive CCP antibodies develop RA." Pet'r's Ex. 25 at 4. Dr. Utz asserted that Dr. Matloubian took Dr. Deane's study out of context and noted that "the EULAR recommendations also noted that an individual should not be classified as having 'preclinical' RA unless they later develop clinical disease." *Id.* at 6. Dr. Utz stated that Dr. Deanne also "note[d] that the naming of different stages of disease development is also controversial." *Id.* Dr. Utz quoted the authors' inability to conclude "whether smoking is an initial trigger for autoimmunity and/or a propagating factor, or even perhaps a permissive factor for some other aetiologic agent such as a bacterial organism." *Id.* He wrote, "experts . . . are actively contemplating the possibility that bacterial triggers, and by inference vaccines, viruses, drugs, and other environmental triggers, play a role in RA. *Id.* Dr. Utz's theory is considered in the context of someone "free from any sort of persistent or recurring polyarticular joint symptoms" that post vaccination, "developed new onset, seropositive, RA." Pet'r's Ex. 17 at 14–15. By a preponderance of the evidence, Petitioner's theory of molecular mimicry does explain how the flu vaccine could in fact cause the development of RA.

C. *Althen* prong two

Although Dr. Utz set out a detailed causation theory, he provided no evidence to link his theory to Petitioner's case. Dr. Utz set out in the conclusion of his final report to apply the facts in Petitioner's case to his causation theory. He wrote, "Petitioner was free from any sort of . . .

symptoms." Pet'r's Ex. 44 at 12. He continued that "[a]lthough she was a smoker, this is not a trigger;" therefore, "[t]he only environmental trigger [he] could identify was the influenza vaccine." *Id.* Dr. Utz wrote in his report that "Dr. Matloubian's argument supports [his] argument that Petitioner had a genetic predisposition to develop RA." Pet'r's Ex. 25 at 3. He later testified that Petitioner was probably DR4 positive. However, he did not discuss what evidence there is of such in her family's history or her medical record. Instead, it appears that he begins with that conclusion and then argues there is no other explanation. Additionally, Dr. Utz did not discuss any evidence that Petitioner was suffering from an acute immune system response to the flu vaccine. He noted that she suffered from immediate shoulder pain, but he was unclear whether her pain resulted from the mechanics of the vaccine administration; and, it is unlikely given the timing that her pain resulted from the onset of her autoimmunity. Dr. Utz agreed with Dr. Matloubian's assertion that "seminal studies [have shown] that autoantibodies and abnormal levels of cytokines are found in blood of patients months or years before they develop clinical RA." *Id.* at 4. He continued, "[h]owever, it is misleading to think that all asymptomatic individuals with abnormal cytokine levels or positive CCP antibodies develop RA." *Id.* Dr. Utz failed to mention at this point that Petitioner did develop RA. In fact, Dr. Utz failed to provide a single example of an instance where clinical symptoms preceded the development of CCP antibodies. He did admit, however, that "Petitioner's course is not atypical." *Id.*

Petitioner's age, race, and gender placed her in a category of individuals with an increased risk for RA. Her years of heavy smoking greatly exacerbated that risk and provided an environmental trigger that both experts agreed is universally accepted in the rheumatological community. Dr. Matloubian testified that it is also universally accepted in the rheumatology community that patients present with clinical symptoms and are diagnosed with RA after a significant amount of time with asymptomatic autoimmunity. Dr. Utz agreed. Furthermore, Dr. Utz presented no evidence that Petitioner experienced symptoms consistent with an immune system reaction to a trigger after years of environmental factors and previous exposure to the flu virus or vaccine. Dr. Utz did not present evidence that other "triggers" had been identified to analogize to Petitioner's vaccination. In fact, both experts agreed that the etiology of RA was unknown. Petitioner's expert focused on her antibody testing to establish the vaccine as a trigger; however, he admitted there is no way to know whether Petitioner became anti-CCP positive before or after vaccination. He also admitted that Petitioner's RF test was not the best indicator of RA autoimmunity.

As a final note to be discussed more thoroughly pursuant to prong three, Petitioner's self-described timing of symptom onset supports Respondent's contention that Petitioner was anti-CCP positive before vaccination. Also, Dr. Utz did not provide a persuasive explanation for how Petitioner's clinical symptoms could manifest one day after her vaccination if molecular mimicry had to occur following the body's recognition of the relevant peptide in the vaccine. In contrast, if Respondent's expert correctly identified Petitioner's symptom onset, Petitioner would not have experienced her first sign of inflammation until six months post vaccination. Either way, the development of Petitioner's symptoms does not support the application of molecular mimicry to Petitioner's case.

D. *Althen* prong three

In his report, Dr. Utz stated that Petitioner's symptoms began one day post vaccination, on October 20, 2013, with soreness in her shoulders. Pet'r's Ex. 17 at 3. He later testified that she "was really struggling the first three days, but then the three to six days." Tr. 66:2. On cross-examination, Dr. Utz committed to onset at day three. Tr. 155:12. During re-direct, Dr. Utz stated that Petitioner "had her first evidence of inflammatory arthritis within the first [thirteen] or so days after her vaccination." Tr. 338:17–19. When I asked Dr. Utz about the onset of Petitioner's symptoms after all his previously quoted testimony, Dr. Utz stated that Petitioner's symptoms began with shoulder pain on the day of vaccination. Tr. 361:23–24. Dr. Utz was then asked whether the shoulder pain was due to the administration of the vaccine or the beginning of autoimmunity. His answer was unclear. Tr. 363:2–364:11. Ultimately, Dr. Utz stated that he [did not] remember if it's within one day or three days, but it's – it's pretty quick." Tr. 364:9–10. When asked whether a three-day onset is significant for his causation theory when compared to a one-day onset, Dr. Utz answered that it is not. Tr. 365:7.

On every occasion that Dr. Utz was asked to clarify Petitioner's onset of symptoms, his response changed. A causation theory that is based on molecular mimicry requires the involvement of the adaptive immune process. There was no literature filed or testimony provided to suggest that cross-reactivity can occur and autoimmunity can develop within twenty-four hours of exposure to the foreign antigen. Dr. Utz attempted to address varying onset dates in his report, stating, "[i]t is likely in [Petitioner's] case that this is a classic example of memory immune response, in which preexisting memory B and T cell were activated by the vaccine." Pet'r's Ex. 17 at 11. He goes on to describe this as "[d]isease triggering [that] may have occurred secondary to formation of immune complexes . . . ." *Id.* Dr. Utz introduced several new mechanisms at this point in his report, but they are not further explained in subsequent writing or testimony. The connection, if any, between molecular mimicry and these immune complexes is never made. Furthermore, Dr. Utz described these phenomena as "scientifically plausible," which is not the standard for the vaccine program. This secondary explanation for the timing of Petitioner's symptom onset lacks development and is inconsistent with Petitioner's main theory of molecular mimicry.

Dr. Matloubian testified that Petitioner first exhibited symptoms of RA "when she saw Dr. Gharda on April 3, 2014, and she documented right knee was swollen and warm." Tr. 248:6–9. He explained that RA is an autoinflammatory disease, meaning the inflammation results from the autoantibody production. Both experts agree that there is no way to know whether Petitioner was anti-CCP positive prior to her test in April of 2014. They agree that in clinical practice, patients often test anti-CCP positive prior to testing positive for RF. Tr. 154:20–21; Tr. 235:18–21. They also agree that anti-CCP testing is more specific for RA than RF. Tr. 154:5–8; Tr. 233:23–24.

Based on the testimony of both experts regarding the development of RA, as well as the literature filed, it is more likely than not that Petitioner's symptoms could have only developed after she experienced autoimmunity. Although Petitioner was not tested for autoantibodies prior to her vaccination, the testimony and literature illustrate her progression from genetic risk at birth, to smoking for several years, to the development of autoimmunity over time, and finally to

the manifestation of symptoms. The timing proposed by Petitioner's expert was inconsistent and too short to reflect an appropriate temporal relationship for Petitioner's RA to be caused by molecular mimicry. Furthermore, Dr. Matloubian's assertion that Petitioner's symptoms manifested six months post vaccination is too long for molecular mimicry to be the cause. Petitioner does not meet her burden under either reading of the facts.

VI. Conclusion

After a review of the record, including Petitioner's medical records, personal statements, expert reports, accompanying literature, and testimony, Petitioner has not proven it is more likely than not that she suffered from a vaccine-caused injury. Petitioner's expert focused on molecular mimicry but identified bystander activation, immune complexes, and others as plausible explanations. Petitioner failed to establish it is more likely than not that her flu vaccination triggered any autoimmune response that lead to her development of RA. Additionally, the onset of her symptoms was muddled by her expert, and his last attempt at clarification under my questioning revealed a temporal relationship that would not be appropriate based on a molecular mimicry theory. Therefore, Petitioner has not satisfied her burden under *Althen*. There is no question about Petitioner's diagnosis of RA, and I reviewed the entire record in order to make a determination whether Petitioner's condition was a result of her vaccination. I could not conclude that it was. Petitioner's claim is hereby **DENIED**.

In the absence of a timely filed motion for review filed pursuant to Vaccine Rule 23, **the Clerk of Court is directed to ENTER JUDGMENT** consistent with this decision.[76]

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master

[76] Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of a notice renouncing the right to seek review.